

## METHODS AND COMPOSITIONS FOR INCREASING

## ANTIBODY PRODUCTION

Reilly et al. Attorney Docket P1957R1

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1 GAATCAACT TCTCCATCT TTGGATAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCC AAAAGAAGA AGAGTGAAT  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGCTG TACTTTTAG AGTAAGACT CAACAATAA TTGACAGGG TTTTCTTCT TCTCAGCTTA

101 GAAGTGTG CGCAGGTAGA AGCTTTGAG ATTATGCTCA CTGCATGCT TGCNATATG GCGAATAATG ACCAAGAGG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTTACGA AGCGTTATAC CGGTTTAC TGGTTGTGC CAACTAAC TA GTCATCTCC

201 GGGCGCTGA CGAGGTAAAG CCCGATGCCA GCATTCTGA CGACGATAG GAGCTGCTGC GCGATTACGT AAGAAGTTA TTGAAGCATC CTCGTCAGTA  
CCCGGACAT GCTCCATTTC GGGTACCGT CGTAAGGACT GCTGCTATGC CTCGACGAG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAG GCGAGACTT ATAGTCGCTT TGTGTTTAT TTTTAATGTA TTTGTAAC TA GTACGCAAGT  
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTGTA TATCAGCGAA ACAAATATA AAATTTAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGGTATCTA GAATTATGAA GAAGATATC GCATTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAACCGGTA CCGTGATATC  
AGTGCAATTT TCCCATAGAT CTTAATCTT CTTCTTATAG CGTAAGAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
~Still Signal Sequence TIR-1 Anti-Tissue Factor Light Chain~

501 CAGATGACC AGTCCCGAG CTCCTGTGTC GCCTGTGTTG GCGATAGGT CACCATCACC TGCAGAGCA GTCCGACAT CAAGAGCTAT CTGAACGTGT  
GTCTACTGG TCAGGGGCTC GAGGACAGG CGGAGACACC CCGTATCCCA GTGGTAGTG AGGTCTCGT CAGCGCTGTA GTTCTCGATA GACTTGACCA

26 Q M T Q S R S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTTA CTATGCTACT AGTCTGCTG TCCAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC  
TAGTTGCTTT TGGTCTTTT CGAGGCTTTC ATGACTAAT GATAGCATGA TCAGACGAC AGTCTCGCT TCTCAGAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y A T S L A E G V P S R F S G S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCAGAGAGAC TTCGCACTT ATTACTGTCT TCAGCAGCA GAGTCTCCAT GGACATTTGG ACAGGGTACC  
CCTAATGTGA GACTGGTAGT CGTCAGACGT CGGCTCTCTG AAGGCTTGA TAATGACAGA AGTCTGCTCT CTAGAGGTA CCGTAAACC TGTCCCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGGTGGGA TCRAACGAC TGTGGGTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TCGTCTGTT GTGTGCTGTC  
TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAGGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACGAAGACAA CACACGAGC

126 K V E I K R T V A A P S V F I F P S D E Q L K S G T A S V V C L L

901 TGAATTAATT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGATAAC GCGTCCAAT CGGTAAC TCAGGAGAGT GTACAGAGC AGGACAGCA  
ACTTATTGAA GATAGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CGGAGGTTA GCGGCTCTCA CAGTCTCTCG TCCTGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1101 GGACGACCC TACAGCCTCA GGACACCTT GACGTGAGC AAGACAGCT ACGAGAAACA CAAGTCTAC GCGTGGAAAG TCACCCATCA GGGCTGAGC  
CCTGTGCTGG ATGTGGAGT CGTCGTGGGA CTGCGACTCG TTGCTCTGA TGTCTTTGT GTTTCAGAT CGGACGCTTC AGTGGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCGCTCA CAAAGAGCTT CAAAGAGGGA GAGTGTAAAT TAAATCCTCT ACGCCGAGC CATGCTGGG AGCTCGGTAC CCGGGATCT AGGCTAAGC  
AGCGGAGCT GTTCTCGAA GTTGCTCCCT CTCACAATA ATTAGAGA TCGGCGCTGC GTAGACCGC TCGAGCCATG GCGCCCTAGA TCGGATTC

226 S P V T K S F N R G E C O

FIG. 1A

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1201 CTCGGTTGCC GCGGGCGGTT TTTTATTGTT GCCAGCGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGAATGCTTT  
GAGCCAACGG CCGCCCGCAA AAAATAACHA CCGGTGCGCG TAGAGCTTAC TTGACAACAG CGTCCATCTT CGAAACCTCT AATAGCACTG ACGTTACGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGGTGTATC GAGTAAAGC CCGATGCCAG CATTCTCTAC GAGATACGG  
CGGTATATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCC CCGCACATG CTCATTTCG GGTACGGTC GTAAGCACTG CTGCTATGCC

1401 AGTGTCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA' AAAGTTAATC TTTTCAACAG CTGTCTATAA GTTGTACGG CCGAGACTTA  
TCGACGACCG GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCATTTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTGCCTTT GTTTTATTTT TTTAATGTAT TTGTAACATG TAGCGAAGTT CAGGTAAAAA GGTATCTAG AATTATGAAG AAGAATATCG CATTCTTCT  
ATCAGCGAAA CAATAATAAA AAATTACATA AACATTGATC ATCGGTCAA GTGCATTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA  
M K K N I A F L L  
\*STII Signal Sequence TIR-1

1601 TGCATCTATG TTCGTTTTTT CTAATGCTAC AAACCGTAC GCTGAGTTTC AGCTGGTGA GTCTGGGGT GGCTGGTGC ACCAGGGGG CTCACTCGGT  
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGGCATG CGACTCCAAG TCGACCACT CAGACCGCCA CCGACACAG TCGGTCCCCC GAGTGAGGCA  
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R  
\*Anti-Tissue Factor Heavy Chain

1701 TTGTCTGTG CAGCTTCTGG CTTCAATATT AAGAGTACT ACATGCACTG GTTCGCTCAG GCCCGGGTA AGGCCCTGA ATGGTTTGA TTGATTGATC  
AACAGGACAC GTCAAGACCG GAAGTTATAA TTCTCTATGA TGTACGTGAC CAGGCGATC CGGGCCCAT TCCCGACCT TACCAACCT AACTAACTAG  
43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

1801 CAGAGCAAG CAACACGATC TATGACCGA AGTTCAGGA CCGTGCCACT ATAAGCGTG ACAATTCCAA AAACACAGCA TACCTGCAGA TGAACAGCCT  
GTCTGCTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTCT GGACGGTGA TATTCGCGAC TGTAAAGTT TTGTGTCTG ATGGAGTCT ACTTGTCCGA  
77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S L

1901 GGTGTCTGAG GACACTGCG TCTATTATTG TGCTCGAGAC ACGCCGCTT ACTTCACATA CTGGGGTCAA GGAACCCCTGG TCACCGTCTC CTCGCCCTCC  
CGCAGACTC CTGTGACGG AGATAATAC ACGAGTCTG TGCCGCGCAA TGAAGCTGAT GACCCCGATT CCTTGGGACC AGTGGCAGAG GAGCCGGAGG  
110 R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V T V S S A S

2001 ACCAAGGCC CATCGTCTT CCGCTTGGA CCGTCTCCA AGACACTC TGCGGCGACA GCGGCCCTGG GCTGCCTGGT CAAGGACTAC TTCCCGGAAC  
TGGTCCCGG GTAGCCAGAA GGGGACCGT GGGAGAGGT TCTGTGGAG ACCCCGCTGT CCGCGGACC CGACGGACCA GTTCTGTATG AAGGGCTTG  
143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P

2101 CGGTGACGT GTCGTGAAAC TCAGGCGCC TGACAGCGG CGTGCACACC TTCCCGGCTG TCTACAGTC CTCAGGACTC TACTCCCTCA GCAGGTGTGT  
GCCACTGCA CAGCACCTTG AGTCCGCGG ACTGTGCGC CACGTGTGG AGGGCGGAC AGGATGTAG GAGTCTGAG ATCAGGAGT CGTCCGACCA  
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V

2201 GACTGTGCC TCTACAGCT TGGGCACCA GACCTACATC TCCAACGTGA ATCACAAGCC CAGCAACACC AAGGTGGACA AGAAGTTGA GCCCAATCT  
CTGACACGG AGATCGTGA ACCGTGGT CTGGATGTAG ACGTTGCACT TAGTGTTCGG GTCTGTGG GTCCACCTGT TCTTCAACT CGGTTTGA  
210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S

2301 TGTGCAAAA CTCACATG CCCACCTGC CCAGCACCTG AACTCTGGG GGGACCGTCA GTCTTCTCT TCCCGCCAAA ACCCAGGAC ACCCTCATGA  
ACACTGTTT GAGTGTATC GGTGGCACG GGTCTGGAC TTGAGGACCC CCTGGCAGT CAGAGGAGA AGGGGGTTT TGGGTTCTG TGGGAGTACT  
243 C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I

2401 TCTCCCGGAC CCTGAGTGC ACATGCGTGG TGGTGGACGT GAGCCACGAA GACCTGAGG TCAAGTTCAA CTGTACCTG GAGGGCGTGG AGGTGCATAA  
AGAGGGCTG GGGACTCCAG TGTAGGACC ACCACCTGA CTCGGTGTCT TGGGACTCC AGTTCAAGTT GACCATGCAC CTCGCGCACC CTCACGTATT  
277 S R T P E V T C V V D V S H E D P E V K F N W Y V D G V E V H N

FIG. 1B

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2501 TCCCAAGACA AAGCGCGGG AGGAGCAGTA CAACAGCAGG TACCGTGTGG TCACGCTCCT CACCGTCTTG CACGAGGACT GGCTGAATGG CAAGAGGTAC  
ACGGTTCTGT TTGCGCGGCC TCCTGCTCAT GTTGTGCTGC ATGCACACCC AGTCGACGGA GTGGTCCTGA CCGACTTACC GTTCTCTCATG  
310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y  
2601 AAGTCAAGG TCTCAACAA AGCCTCCCA GCGCCCATCG AGAAACCAT CTCCAAGCC AAAGGCGAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC  
TTCAGTTCC AGAGTTGTT TCGGGAGGT CCGGGGTAGC TCTTTGGTA GAGTTTCGG TTTCGCTGG GGGCTCTTGG TGTCACATG TGGGACGGGG  
343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P  
2701 CATCCCGGA AGAGATGACC AAGAACCAGG TCAGCTGAC CTGCTGTGC AAAGGTTCT ATCCAGCGA CATGCCGTG GAGTGGGAGA GCAATGGGCA  
GTAGGCCCT TCTCTACTGG TTCTTGCTCC AGTCGACTG GACGACCCAG TTTCGGAAGA TAGGTCGCT GTAGCGGCAC CTCACCTCTT COTTTACCGT  
377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q  
2801 GCGGAGAAC AACTACAAGA CCAGCCTCC CGTGTGGAC TCCGACGGCT CTTTCTTCT CTACAGCAAG CTCACCGTGG ACAAGAGCAG GTGGCAGCAG  
CGCCTCTTG TTGATGTTCT GTTGGGAGG GCACGACCTG AGGCTGCCGA GGAAGAAGGA GATGCTGTC GAGTGGCACC TGTCTCTGTC CACCTCTGTC  
410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q  
2901 GSGAAGTCT TCTCATGCTC CGTGATCAT GAGGCTCTGC ACAACCACTA CAGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATGAAGA TCCGACGGCC  
CGCTTGCGA AGAGTACGAG GCACTACGTA CTCGAGAGG TGTTGTGAT GTGGCTTTC TCGGAGAGG ACAGAGGCC ATTTATTCTG AGCCTGCCGG  
443 G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K O  
3001 CTAGAGTCCC TAACGCTCGG TTGCGCGCGG GCGTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG TTTATCACAG  
GATCTCAGG ATTGGAGCC AACGGCGGCC CGCAAAAAT AACATTGAG TACAAACTGT CGAATAGTAG CTATTGAAA TTACGCCATC AATATGTGC  
3101 TTAATTTGCT AACGAGTCA GGCACCGTGT ATGAAATCTA ACAATGCGCT CATGTCATC CTCGGCACCG TCACCTGGA TGCTGTAGGC ATAGCTTGG  
AATTTAACGA TTGCTCAGT CCGTGGCACA TACTTTAGAT TGTTACGCGA GTAGCAGTAG GAGCGGTGGC AGTGGGACCT ACGACATCCG TATCCGAACC  
^Start Tet Resistance Coding Sequence  
3201 TTATGCCGT ACTGCCGGC CTCTTGCGG ATATCGTCCA TTCCGACAGC ATGCCAGTC ACTATGGCT GCTGTAGCG CTATATGCGT TGATGCAATT  
AATACGCCA TGACGGCCG GAGAACGCC TATAGCAGT AAGGCTGTG TAGCGTCTG TAGTACCGCA CGACATCGC GATATACGCA ACTAGCTTAA

3301

FIG. 1C

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1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATT TTTTCTTCT TCTCAGCTTA  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTCG TACTTTTAG AGTAACGACT CAACAATAA TTGGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACAGC GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACCTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGAGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGTCAGTA  
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACCTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACAA GCTGTCATAA AGTTGTACAG GCCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT  
TTTTCAATTA GAAAAGTTGT CGACGTAAT TCACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATCGGTTCA

401 TCACGTAAAA AGGTATCTA GAAATTATGAA GAAAAACATC GCTTTCTTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC  
AGTGCAATTT TCCCATAGAT CTTAATACCTT CTTTGTAG CGAAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K N I A F L L A S M F V F S I A T N A Y A D I  
^start STII signal TIR-2 start light chain^

501 CAGATGACCC AGTCCCGCAG CTCCTCTGTC GCTCTGTGG CGATAGGGT CACCATCACC TGCAGAGCCA GTGCGGACAT CAAGAGCTAT CTGAACCTGGT  
GTCTACTGGG TCAGGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTG AGCTCTCGT CAGCGTGTA GTTCTCGATA GACTTGACCA

26 Q M T Q S P S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAAA GCTCGAAAG TACTGATTTA CTATGCTACT AGTCTCGTG AAGAGTCCC TTCTCGTTC TCTGATCGG GTTCTGGAC  
TAGTTGTCTT TGGTCTTTT CGAGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCCTCAGG AAGAGCGAAG AGACCTAGSC CAAGACCCTG

60 Q Q K P G K A P K V L I Y A T S L A E G V P S R F S G S G S T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTTGG ACAGGTATCC  
CCTAATGTA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCTGCTCT CTCAGAGGTA CCTGTAAACC TGTCCCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGT GTGTGCTGC  
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGATTAAC GCCCTCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA  
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACTT CCACCTATTG CGGAGGTTA GCCCATGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCTCA GCAGCACCTT GAGCTGAGC AAGCAGACT ACGAACA CAAAGTCTAC GCCTGGAG TCACCCATCA GGGCCTGAGC  
CCTGCTGG AGTCTGGAGT CGTCTGGGA CTGCGACTCG TTTCTCTGA TGTCTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

FIG. 2A

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1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GAGCGTGAGC AAGCAGACT ACGAGAAACA CAAAGTCTAC GCGTGGAG TCACCCATCA GGGCGTGAGC  
CCTGTGCTGG ATGTCGAGT CGTCGTGGGA CTGCGACTCG TTCTCTCTGA TCCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCCGGACTCG  
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTT ACGCCGAGC CATCGTGCG AGCTCGGTAC CCGGGGATCT AGGCCTAAACG  
AGCGGGCAGT GTTCTCGAA GTTGTCCCTT CTCACAAATTA ATTAGGAGA TCGGGGCTGC GTAGACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC  
226 S P V T K S F N R G E C O

1201 CTGCGTTGCC GCGGGGCGTT TTTTATTGTT GCGGACGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT  
GAGCCACCG CGGCCGCA AATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGG GCGGTGTATC GAGTAAAGC CGATGCGCAG CATTCCTGAC GACGATACGG  
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAATAG TCCATCTCCC CGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGTGTGCTGG CGATTAGGTA AGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAG CCGAGACTTA  
TCGACGACGC GCTAATGCAT TTCTCAATA ACTTCGTAGG AGCATCAT TTTCATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TACGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAG AAAAACATCG CTTTCTTCT  
ATCAGCGAAA CAAAATATAA AATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATACTTC TTTTGTAGC GAAAAGAAGA  
1 M K N I A F L L  
^start Still signal TIR-2

1601 TGCATCTATG TTCGTTTTTT CTATTGCTAC AAACGGTAC GCTGAGGTT AGCTGGTGA GTCTGGCGGT GGCCTGGTGC AGCCAGGGGG CTCACTCCGT  
ACGTAGATAC AAGCAAAAA GATAACGATG TTGCGCATG CGACTCCAAG TCGACCACT CAGACCGCA CCGGACCAAG TCGGTCCGCC GAGTGAGGCA  
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G S L R  
^start heavy chain

1701 TTGCTCTGTG CAGTTCTGTG CTTCAATATT AAGGATACT ACATGCACTG GGTCCGTGAG GCGCCGGGTA AGGGCTTGA ATGGTGTGA TTGATTGATC  
AACAGGACAC GTCGAGAC GAACTTATAA TTCTCTATGA TGTACGTGAC CCAGGAGTC CGGGGCCCCAT TCCCGACCT TACCCAACCT AACTAAGTAG  
43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

1801 CAGAGCAAGG CAACAGATC TATGACCGA AGTTCAGGA CCGTGCCACT ATAAGCGCTG ACATTTCAA AAACACAGCA TACCTGCAGA TGAACAGCCT  
GTCTCGTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTT GGCACGTGA TATTGCGAC TGTAAAGTT TTTGTGCTGT ATGACGCTCT ACTTGTGGA  
77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S L

1901 GCGTGTGAG GACACTGCCG TCTATTATTG TGCTGAGAC ACGGCCGCTT ACTTGACTA CTGGGTCAA GGAACCTGG TCACCGTCTC CTCGGCCTCC  
CGCACGACTC CTGTGACGC AGATAATAAC ACGAGTCTG TGCCGGCGAA TGAAGTAT GACCCAGTT CTTGGGACC AGTGGCAGAG GAGCGGAGG  
110 R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V T V S S A S

2001 ACCAAGGCC CATCGTCTT CCCCTGGCA CCTCTCCA AGACACCTC TGGGGCACA GCGGCCCTGG GCTGCTGTGT CAAGGACTAC TTCCCGAAC  
TGGTTCCGG GTAGCCAGAA GGGGACCGT GGGAGGAGT TCTGTGAG ACCCCGTTG CCGCGGACC CGACGAGCA GTTCTGATG AAGGGCTTG  
143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P

2101 CGGTGACGTT GTCGTGGAAC TCAGGCGGCC TGACACGCG GGTGCACACC TTCCGGCTG TCCTACATGCT CTCAGGACTC TACTCCCTCA GCAGGTGTT  
GCCACTGCCA CAGCACCTTG AGTCCGCGG ACTGTCGCC GCAGTGTGG AAGGCCGAC AGGATGTGAG GAGTCTGAG ATGAGGAGT CGTGCACCA  
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V

FIG. 2B

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2101 CGGTGACGGT GTGTGGAAC TCAGGCGCCC TGACGACCGG CGTGACACCC TTCCGGGTG TCCTACAGTC CTCAGSACTC TACTCCCTCA GCACGCTGGT  
GCCACTGCCA CAGCACCTTG AGTCCGCGGG ACTGTCGCC GCACGTGG GCACGTGG AAGGCCGAC AGGATGTCAG GAGTCTCTGAG ATGAGGGAGT CGTCGCACCA  
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V  
2201 GACTGTGCC TCTAGCAGT TGGGCACCCA GACCTACATC TGCAACGTGA ATCAACGCC CAGCAACACC AAGTGGACA AGAAAGTTGA GCCCAATCT  
CTGACACGGG AGATGTCGA ACCCGTGGT CTGATGTAG AGTTGACT TAGTGTGG GTCTGTGG TTCCACCTGT TCTTCACT CGGGTTTGA  
210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S  
2201 TGTGACAAA CTCACACATG CCCACCGTC CCAGCACCTG AACTCTGG GGGACCTCA GTCTCTCT TCCCCCAA ACCCAAGGAC ACCCTCATGA  
ACACTGTTT GAGTGTGAC GGGTGGCAG GGTCTGGAC TTGAGGACC CCCTGGCAGT CAGACGAGA AGGGGGTTT TGGGTCTCTG TGGGAGTACT  
243 C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I  
2401 TCTCCGGAC CCCTGAGTC ACATGCTGG TGTGGACGT GAGCCAGAA GACCTGAG TCAAGTTCAA CTGTACGTG GACGGCTGG AGTGCATAA  
AGAGGCTG GGGACTCCAG TGTACGCACC ACCACTGCA CTGGTCTT CTGGACTCC AGTTCAAGTT GACCATGCAC CTGCCGACC TCCACGTATT  
277 S R T P E V T C V V D V S H E D P E V K F N W Y V D G V E V H N  
2501 TGCCAAAGACA AAGCGCGG AGGAGCAGTA CAACAGCAG TACCGTGTG TCAGGTCT CACCGTCTG CACCAAGACT GGCTGAATGG CAAGGAGTAC  
ACGGTCTGT TTGCGCGCCC TCCTGTCAT GTTGTGTC AGTGACACC AGTGACAGG GTGGCAGGAC GTGTCTCTGA CCGACTTACC GTTCTCTCATG  
310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y  
2601 AAGTGAAGG TCTCAACAA AGCCCTCCA GCCCCTATG AGAAACCAT CTCCAAAGC AAAGGCGAG CCGAGAGACC ACAGGTGTAC ACCCTGCCC  
TTACGTTCC AGAGTTGT TTGCGGAGGT CCGGAGGTAG TCTTTGTA GAGTTCTG TTTCCTGTCG GGGTCTTGG TGTCACATG TGGGACGGG  
343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P  
2701 CATCCCGGA AGAGTACC AAGAACCG TCAGCTGAC CTGCTGTGTC AAGCTTCT ATCCAGCGA CATCGCCCTG GAGTGGAGA GCAATGGSCA  
GAGGGCCCT TCTCTACTG TTCTTGTCC AGTCGACTG GAGGAGCAG TTTCGAGA TAGGTCTGT GTAGCGGAC CTCACCTCT CGTTACCCGT  
377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q  
2801 GCGGAGAAC AACTACAAGA CCACGCTCC CGTGTGGAC TCGACGGCT CTTCTTCT CTACAGCAG CTCACCGTGG ACAAGAGCAG GTGGCAGCAG  
CGGCTCTTG TTGATGTTT GTGCGGAGG GCACGACTG AGGCTGCCA GGAAGAAGA GATGCTTC GAGTGGCACC TGTTCTCGTC CACGTCGTC  
410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q  
2901 GGGAACTCT TCTATGCTC CGTATGAT GAGCTCTGC ACAACACTA CACGACAG AGCTCTCC TGTCTCCGG TAAATAAGCA TGGACGGCC  
CCCTTGACA AGATACGAG GCACTACGTA CTCGACGTA TGTGTTGAT GTGCTCTTC TCGGAGAGG ACAGAGGCC ATTTATCGT ACGTGGCCG  
443 G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K O  
3001 CTAGAGTCC TAACGCTCG TTGCGCGCG CGGTTTTTA TTGTTAACTC ATGTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG TTTATCACAG  
GATCTCAGG ATTGCGAGC AACGGCGGCC CGCAAAAT AACAACTG TACAACCTG CGAATAGTAG CTATTCGAAA TTACGCCATC AATAGTGTG  
3101 TTAATTTGCT AACGAGTCA GGCACCTGT ATGAATCTA ACAATGCT CATGCTATC CTCGGCACC TCACCTGGA TGCTGTAGG ATAGGCTTGG  
AATTTAAGA TTGCTCAGT CCGTGGACA TACTTAGAT TGTACCGA GTAGCAGTAG GAGCCGTGGC AGTGGAGCT ACGACATCCG TATCCGAAAC  
3201 TTATGCGGT ACTGCGGGC CTCTGCGGG ATATGTTCA TT  
AATACGGCCA TGACGGCCC GAGAACGCC TATAGAGGT AA

FIG. 2C

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1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTATT TTAGCTTGCC AAAAAGAAGA AGAGTCGAAT  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGCTG TACTTTTAG AGTAACGACT CAACAATAA TTGGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGT GCGAGGTAGA AGCTTTGGAG ATTATCCTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTTACGA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGA CGAGGTAAAG CCCGATGCCA GCATTCTGTA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTGAGTA  
CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACA GCTGTCAATA AGTTGTACAG GCGGAGACTT ATAGTCGCTT TGTTTTATT TTTTAAATGA TTTGTAATA GTACGCAAGT  
TTTTCAATTA GAAAGTTGT CGACAGTATT TCACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCAGTAAAA AGGGTATCTA GAATTATGAA GAAGAAATAT GCATTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAACGCGTA CCGTGATATC  
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCCTTAG COTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG  
1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
\*stII Signal TIR -1 Anti-VEGF Light chain\*

501 CAGTTGACCC AGTCCCGAG CTCCTGTGTC GCGTAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAACACTGGT  
GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCA GTGCTAGTG AGCTGCGTT CAGTCTTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCGAAAG TACTGATTTA CTTCACTCC TCTCTCACT CTGAGTCCC TTCTGCTTC TCTGATCCG GTTCTGGAC  
TAGTTGCTT TGGTCTTTT CGAGGCTTTC ATGACTAAT GAAGTGAAG AGAGAGTGA GACCTCAGG AAGAGCGAAG AGACTTAGC CAAGACCTTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGAATTCAT CTGACCATCA GCAGTCTGCA GCGAAGAG TTCGAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGT GGAAGTTGG ACAGGTATCC  
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTCTG AAGCGTTGAA TAATGACAGT TGTCTATAG TGGCAGCGCA CTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAACGAAC TGTGGGTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGTCTCTGTT GTGTGCTCTG  
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTACAGAGA AGTAGAGGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACAGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATTAAT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGGTAAAC GGCTCCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA  
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACTT CCACCTATT GCGGAGGTTA GCGCTCTCA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCAC TACAGCTCA GACGACCTT GACGTGAGC AAAGCAGACT ACGAAGAAAC CAAGTCTAC GCGTGGAAAG TCACCCATCA GGGCTGAGC  
CCTGTGCTGG ATGTGCGAGT CGTGTGGGA CTGCACTCG TTTGCTGTA TGTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGAGCTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTAAAT TAAATCTCT AGCCGAGC CATCGTGGC AGTCTGGTAC CCGGGATCT AGGCTTAACG  
AGCGGGCAGT GTTCTCGAA GTTGCCCTCT CTCACATTA ATTTAGAGA TCGCGCTGCG GTAGCACC CGCCCTTAGA TCCGGATTGC

226 S P V T K S F N R G E C O

FIG. 3A

METHODS AND COMPOSITIONS FOR INCREASING  
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1201 CTGGTTGCC GCGGGCGTT TTTTATTGT GCGAGCGCG ATCTCGAATG AACTGTGTG GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT  
GAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTCGCG TAGAGCTTAC TTGACACAG CGTCCACTCT CGAAACCTCT AATAGCAGTG ACGTTACGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGG GGGGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG  
GGTTATACC GGGTTTACT GGTGTGCGC AACTAAGTAG TCCATCTCCC CCGGACATG CTCCTATTGG GGCTACGGTC GTAGGAGCTG CTGCTATGCC

1401 AGCTGCTGG CGATTACGTA AGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAG CCGAGACTTA  
TGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTCGCTTT GTTTTATT TTAAATGAT TTGTAAGTAG TACGCAAGTT CAGCTAAAGA GGTATCTAG AATTATGAG AAGAATATCG CATTCCTCT  
ATCAGCGAAA CAAAATAAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA  
M K K N I A F L L  
\*STII signal TIR-1

1601 TGCATCTATG TTGTTTTTTT CTATTGCTAC AAACGGTAC GCTGAGTTC AGTGTGGA GTCTGGCGT GGCTCGGTG AGCCAGGGG CTCACTCGT  
ACGTAGATAC AAGCAAAAGA GATAAGATG TTGCGCATG CGATCCNAG TCGACCACCT CAGACCGCA CCGGACCG TGGTCCCCC GAGTGAGCA  
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R  
\*Anti-VBGF Heavy Chain

1701 TTGTCCTG GAGCTTCGG CTAGCACTC AGCACTAG GTATGAAGT GTTCCTGAG GTCCTGGTA GTCTGGCGT GGCTCGGTG AGCCAGGGG CTCACTCGT  
AACAGACAC GTCAAGACC GATGCTGAAG TCGGTGATG CATACTGAC CCAGGAGTC GGGGCCCAT TCCGGACCT TACCAACCT ACCTAATGT  
43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T

1801 CCTATACGG TGAACCGACC TATGCTGCG ATTTCAAGC TGTGTTCACT TTTTCTTTAG ACACCTCAA AAGCAGCA TACCTGCAGA TGAACAGCT  
GGATATGCC ACTTGGCTGG ATAGAGGCC TAAAGTTGC AGCAAGTGA AAAAGAAATC TGTGAGGTT TTGCTGCTGT ATGGAGCTCT ACTTCTCGGA  
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

1901 GCGCGCTGAG CACACTGCG TCTATTACTG TGCAAAGTAC CCGTACTATT ACGGACGAG CCACTGTAT TTGACGCTT GGGGTCAAG AACCTGTGTC  
CGCGGACTC GTGTAGCGC AGATATGAC ACGTTTCA GGCATGATA TGGCTGCTC GGTGACCAT AAGCTGCAGA CCCCAGTTCC TTGGGACGAG  
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V

2001 ACCGTCTCT CCGCTCCAC CAAGGCCCA TCGGTCTTC CCGTGCACC CTCTCCAG AGCACCTCTG GGGGACAGC GGCCTGGGC TGCCTGTCTA  
TGGCAGAGA GCGGAGGTG GTTCCCGGT ACCCAGAGG GGGACCTGG GAGGAGTTC TCGTGGAGAC CCGGTGTG CCGGACCGG ACGSACCACT  
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

2101 AGGACTACT CCGCAACCG GTGACGGTG GTGGAATC AGGCGCCTG ACCAGCGGG TGCACACCTT CCGGCTGTC CTACAGTCT CAGGACTCTA  
TCTGATGAA GGGGCTTGG CACTGCCACA GCACCTGAG TCGCGGGAC TGGTCCCGC ACGTGTGAA GGGGACAGC GATGTCAGA GTCTGTGAT  
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCTCAGC AGCGTGTGA CTGTGCCCTC TAGCAGCTG GGCACCCAGA CCTACATCTG CAAGTGAAT CACAAGCCCA GCAACACCAA GGTGACAAAG  
GAGGAGTCT TCGACCACT GACACGGAG ATCGTCGAAC CCGTGGTCT GATGTAGAC GTTGACTTA GTTGTGGT CCGTGTGTT CCACCTGTT  
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACATGCC CACGTCGCC AGCAGCTGAA CTCCTGGGG GACGTCAGT CTTCCTCTTC CCCCAGAAC  
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGACGG GTGCGAGGG TCGTGGACTT GAGACCCCC CTGGAGTCA GAAGGAGAG GGGGTTTG  
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CCTCATGATC TCCCGACCC CTGAGTCTAC ATGCGTGGT GTGGAGTGA GCCACGAAGA CCTGAGGTC AAGTCAACT GGTACGTGGA  
GGTCTCTGT GGAGTACTAG AGGCGCTGG GACTCCAGT TACGACCAAC CACTGCACT CCGTCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACT  
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

FIG. 3B



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2501 CGCGGTGGAG GTGCTAATG CCAAGACAAA GCCGCGGGAG GAGCAGTACA ACAGACGCTA CCGTGTGGTC AGCGTCCTCA CCGTCCTGCA CCAGGACTGG  
GCCGCACTC CAGGTATTAC GGTCTGTTT CGCGCCCTC CTCGTCATGT TGTGTCGAT GGCACACCAG TCGCAGGAGT GGCAGGAGT GGTCTCTGACC  
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W  
2601 CTGAATGGCA AGGAGTACAA GTGCAAGTTC TCCAAAGG CCGTCCCGC CCCATCGAG AAACCATCT CCAAGGCCAA AGGCAAGCCC CGAGAACCAC  
GACTTACCGT TCCTCATGTT CAGGTTCCAG AGGTGTTTC GGGAGGTCG GGGTAGCTC TTGTGTAGA GGTTCGGTT TCCGTCGGG GCTCTTGGTG  
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q  
2701 AGGTGTACAC CTTGCCCCCA TCCCGGAG AGATGACAA GAACAGGTC AGCTGACT GCCTGTGCTA AGCTTCTAT CCCAGCGACA TCGCGGTGGA  
TCCACATGTG GAGCGGGGT AGGGCCCTC TCTACTGTT TCTGTGCTG CCGACTGGA CGACCACTT TCCGAAGATA GGTGCGCTGT AGCGCACCT  
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E  
2801 GTGGGAGAGC AATGGGCAGC CGGAGAACA CTACAAGACC AGCCTCCCG TCGTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGT CACGTTGGAC  
CACCTCTCG TTACCGGTG GCCTCTGTT GATGTTCTG TCGGAGGCG ACACCTGAG GCTGCCGAGG AAGAAGGAGA TGTGTTTCA GTGCGACCTG  
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D  
2901 AAGAGCAGGT GGCAGCAGG GAACTCTTC TCATGCTCCG TGATGCATGA GCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA  
TTCGTCCTCA CCGTGTCCC CTTGCAGAG AGTACGAGG ACTACTACT CCGACAGTG TTGTGATGT GCGTCTCTC GGAGAGGAG AGAGGCCAT  
443 K S R W Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K  
3001 AATAAGCATG CGACGGCCT AGAGTCCCTA ACCTCGGT GCGCGCGGC GTTTTTATT GTTAACTCAT GTTTGACAG TTATCATGA TAAGCTTTAA  
TTATTCGTAC GCTGCCGGA TCTCAGGAT TCCGAGCAA CGCGCGCCG CAAAAAATAA CAATTGAGTA CAACTGTCTG AATAGTAGT ATTGAAATT  
477 O  
3101 TCGGTAGTT TATCAGAGTT AAATTGCTAA CGAGTCAG CACGTGTAT GAATCTAAC AATGGCTCA TCGTCATCT CCGCACCGTC ACCCTGGATG  
ACGCCATCAA ATAGTGTCAA TTACGATT CCGTCAGTCC GTGGCACATA CTTTAGATTG TTACCGAGT AGCAGTAGGA GCCGTGGCAG TGGGACCTAC  
\*Start Tet Resistance Coding Sequence  
3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TCGCGGGCCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCAGTCA TATGGCTGC TGCTAGCGCT  
GACATCCGTA TCCGACCAA TACGGCCATG ACGGCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTGTA GCGGTAGTG ATACCGCAG ACGATCCGGA  
3301

FIG. 3C

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1 GAATTCAACT TCTCCATACT TTGGATAAGG AATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AGCTTGCCC AAAAAGAAGA AGAGTCGAAT  
 CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTCG TACTTTTAG AGTAACGACT CAACAATAA TTGGAACGGG TTTTCTTCT TCTCAGCTTA  
 101 GAACTGTGT GCGAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG  
 CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGCTTATAC CCGTTTAC TGGTTGTGCG CAACTAACCTA GTCCATCTCC  
 201 GGGCGCTGTA CGAGGTAAAG CCGGATGCCA GCATTCCTGA CGACGATACG GAGCTGTGCG GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA  
 CCCCGACAT GCTCCATTTC GGGCTAGGCT CGTAAGGACT GTGCTATGC CTGACGACGG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT  
 301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTGTACAG GCGGACCTT ATAGTCGCTT TGTTTTAT TTTTAATGTA TTTGAACCTA GTACGCAAGT  
 TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA  
 401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAAACGCTA CGCTGATATC  
 AGTGCATTTT TCCCATAGAT CTTAATACCT CTTCTTATAG CGTAAGAAG AAGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG  
 1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
 ^STII Signal TIR -1 ^light chain  
 501 CAGTTGACCC AGTCCCGCAG CTCCCTGTCC GCCTCTGTGG GCGATAGGT CACCATCACC TGCACGCGAA GTCCAGGATAT TAGCAACTAT TTAAACTGGT  
 GTCAACTGGG TCAGGGGCTC GAGGGACAGG CCGAGACACC CGCTATCCCA GTGCTAGTGG ACCTGCGGT CAGTCCCTATA ATCGTTGATA AATTGACCA  
 26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y  
 601 ATCAACAGAA ACCAGSAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCACT CTGGAGTCCC TTCTGCTTC TCTGGATCCG GTTCTGGAC  
 TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGTGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAAGACCTG  
 60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T  
 701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCGAGAAGAC TTCGCAACTT ATTACTGCTA ACAGTATAGC ACCGTGCCGT GGAGCTTTGG ACAGGGTACC  
 CCTAAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CCTGCAAAACC TGTCCCATGG  
 93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T  
 801 AAGGTGGAGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGTCTTCTGT GTGTGCTGC  
 TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CCGTAGACTA CTCGCTCACT TTAGACCTTG ACGAAGACAA CACACGGACG  
 126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L  
 901 TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGAA GGTGGATAAC GGCCTCCAAT CCGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA  
 ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGCTACCTT CCACCTATTG CCGGAGTTA GCGCCTCTCA CAGTGTCTCG TCCTGTGCTT  
 160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K  
 1001 GGACAGCAC TACAGCCTCA GCAGCACCTT GAGCTGAGC AAGCAGACT ACGAGAAACA CAAAGTCTAC GCTGCGAAG TCACCCATCA GGGCCTGAGC  
 CCTGCTGAGG ATGTCGAGT CGTCGTGGA CTGCGACTCG TTTGCTCTGA TGTCTTTGT GTTTCAGATG CCGACGCTTC AGTGGGTAGT CCCGGACTCG  
 193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

FIG. 4A

1001 GGACAGCACC TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAGCAGACT ACGAGAACA CAAGTCTAC GCCTGGAG TCACCCATCA GGGCCTGAGC  
CCTGCTGG AGTCTGGAGT CGTCTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTGT GTTCAGATG CGGACGCTTC AGTGGGTAGT CCGGACTCG  
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S  
1101 TCGCCGCTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCTCTT ACGCCGGACG CATCGTGSCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG  
AGCGGGCAGT GTTCTCGAA GTTCTCCCT CTCACATTA ATTTAGGAGA TCGCGCTGC GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC  
226 S P V T K S F N R G E C O  
lambda t0 terminator  
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCGGACGCG ATCTCGAATG AACTGTGTGC GAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT  
GAGCCAAACG GCGCCGCGAA AAAATAACAA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGT ACGTACGAA  
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GGGCTGTATC GAGGTAAAGC CCGATGCCAG CATTCTGTAC GACGATACGG  
GGTTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCATCTCCC CCGGACATG CTCCATTTG GGTACGGTC GTAAGGACTG CTGCTATGCC  
1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACCG CCGAGACTTA  
TCGACGACG GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAT TTTCATTTAG AAAAGTTGTC GACAGTATT CAACAGTGCC GGCTCTGAAT  
1501 TAGTCGCTTT GTTTTATT TTTAATGTAT TTGTAACATG TAGGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAG AAGAATATCG CATTCTTCT  
ATCAGCGAAA CAAAATATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCCATAGATC TTAATCTTC TTCTTATAGC GTAAAGAAGA  
M K K N I A F L L  
\*STII Signal TIR-1  
1601 TGCACTATG TTCTGTTTTT CTATTGCTAC AAACGCGTAC GGTAGGTTT AGCTGTGGA GTCTGGCGGT GGCCTGTGTC AGCCAGGGG CTCACCTCGT  
ACGTAGATAC AAGCAAAATA GATACGATG TTTCGGCATG CGACTCCAAG TCACCACTT CAGACCGCCA CCGGACACAG TCGTCTCCCC GAGTGAGCA  
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R  
\*start heavy chain  
1701 TTGCTCTG CAGCTTCTGG CTATACCTTC ACCAATATG GTATAAATG GGTCTGCTAG GCGCCGGTGA AGGCTCTGGA ATGGTTGGA TGGATTAAACA  
AACAGGACAC GTCGAAGACC GATATGGAAG TGTTGATAC CATATTGAC CCAGGACATC CCGGCGCCAT TCCTGACCT TACCCAACT ACCTAATGT  
43 L S C A A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T  
1801 CCTATACCG TGAACCGACC TATGCTGCG ATTTCRAACG TCGTTTCACT TTTCCTTTAG ACACCTCCAA AAGCAGCA TACCTGCAGA TGAACAGCCT  
GGATATGCC ACTTGGCTG ATACAGCC TAAAGTTGC AGCAAGTGA AAAAGAAATC TGTGAGGTT TTCTGTCTGT ATGACGCTCT ACTTGTGGA  
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L  
1901 GCGCGCTGAG GACACTGCG TCTATTACTG TGAAGATAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGGTATT TCGACGCTG GGTCAAGGA  
CGCGGACTC CTGTGACGGC AGATAATGAC AGTTTTCATG GGCCTGATAA TACACTTGT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCT  
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G  
2001 ACCTGTGTC CCGTCTCTC GGCCTCCACC AAGGGCCCAT CGTCTTCCC CCGTCCACCC TCCTCCAGA GCACCTCTGG GSGCACAGCG GCCCTGGCT  
TGGACACAGT GGCAGAGGAG CCGAGGTGG TTCCCGGTA GCCAAGGG GACCGTGG AGGAGTTCT CGTGAGACC CCGTGTGCG CCGGACCCGA  
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C  
2101 GCTGTGTC GACTACTTC CCGAAGCGG TGACGTGTC GTGAATCA GCGCCCTGA CAGCGCGT GCACACTTC CCGGCTGTCC TACAGTCTC  
CGGACAGTT CCTGATGAAG GGGCTTGCC ACTGCCACAG CACTTGAGT CCGCGGACT GGTGCGCGA CGTGTGAAG GCGGACAG ATGTCAGGAG  
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S

FIG. 4B

METHODS AND COMPOSITIONS FOR INCREASING  
ANTIBODY PRODUCTION

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2101 GCCTGGTCAA GGACTACTTC CCGAACCGG TGACGGTGTG GTGGAACCTA GCGCCCTGTA CCACGGCGGT GCACACCTTC CCGGCTGTCC TACAGTCCTC  
CGGACCAAGT CCTGATGAAG GGGCTTGGCC ACTGCCACAG CACTTGAGT CCGCGGACT GGTGCGGCA CGTGTGGAAG GCGCGACAGG ATGTCAGGAG  
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S  
2201 AGGACTCTAC TCCTCAGCA GCGTGGTGAC TGTGCCCTCT AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCGAG CAACACCAAG  
TCCTGAGATG AGGGAGTCGT CGCACCACTG ACACGGGAGA TCGTCGAACC CGTGGGTCTG GATGTAGACG TTGCACTTAG TGTTCGGGTC GTTGTGGTTC  
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K  
2301 GTGGACAAGA AAGTTGAGCC CAATCTTGT GACAAACTC ACATGCCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTCAATC TTCCTCTTCC  
CACTGTCTT TCAACTCGG GTTTAGAACA CTGTTTGG TGTGTACGG TGGCAGGGT CGTGGACTG AGGACCCGCC TGGCAGTCAG AAGGAGAAG  
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P  
2401 CCCCAAAACC CAAGGACACC CTCATGATCT CCCGACCCC TGAGGTACA TGCGTGGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG  
GGGTTTGG GTTCTGTGG GAGTACTAGA GGGCCTGGG ACTCCAGTGT AGCACCAACC ACTGCACTC GGTGTTCTG GGAATCCAGT TCAAGTTGAC  
277 P K P K D T L M I S R T P E V T C V V D V S H E D P E V K F N W  
2501 GTAGTGGAC GCGTGGAGG TGCATAATGC CAAGACAAG CCGGGGAGG AGCAGTACA CAGCAGGTAC CGTGTGTCA GGTCTCTCAC CGTCTGCAC  
CATGCACTG CCGCACTCC ACATATTAG GTTCTGTTT GCGGCCCTCC TCGTCATGTT GTCTGTGATG GCACACCACT CCGCAGAGTG GCAGGACGTG  
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H  
2601 CAGGACTGGC TGAATGGCAA GGAGTACAAG TGCAAGTCT CCACAAGC CCTCCAGCC CCATCGAGA AACCATCTC CAAAGCCAAA GGCAGGCCCC  
GTCTGACCG ACTTACCGTT CCTCATGTT ACCTGTTCCAGA GGTGTTTCG GGAGGTTCG GGTGATCTT TTTGGTAGG GTTTCGGTTT CCGTCGGGG  
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R  
2701 GAGAACACA GGTGTACACC CTGCCCCAT CCGGGAAGA GATGACCAAG AACCAAGTCA GCTGACCTG CCTGGTCAA GGCTTCTATC CCACGACAT  
CTCTTGGTGT CCACATGTT GACGGGGTA GGGCCCTTCT CTACTGTTTCT TTGTCCAGT CCGACTGGAC GGACCAAGTT CCGAAGATAG GGTGCTGTA  
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I  
2801 CCGCTGGAG TGGGAGACA ATGGGACGCC GGAGAACAC TACAAGACA CCGCTCCCGT GCTGGACTCC GACGGTCTCT TCTTCTCTA CAGCAAGCTC  
GGGGACCTC ACCCTCTCGT TACCCGTCCG CCTCTTGTG GTGTTCTGTT GCGGAGGGA CAGCTGAGG CTGCGGAGGA AGAAGGAGAT GTGCTTCGAG  
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L  
2901 ACCGTGGACA AGACAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATCATGAG GCTCTGACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT  
TGGCACCTGT TCTGTTCCAC CGTGTCTCCC TTGACAGAAGA GTACGAGGCA CTACGTACTC CGAGAGGTGT TGGTGTATG CGTCTTCTCG GAGAGGACA  
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S  
3001 CTCGGGTAA ATAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCGGGGG TTTTATTG TTAACATCAT TTTGACAGCT TATCATCAT  
GAGGCCATT TATTCGTAGC CTGCGGGAT CTCAGGGATT GCGAGCAAC GCGGCCCGC AAAAAATAAC AATTGAGTAC AAATGTGCA ATAGTAGCTA  
477 p G K O  
^lambda terminator  
3101 AAGCTTTAAT GCGTAGTATT ATCAGATTA AATTGCTAAC GCAGTCAGGC ACGTGTATG AAATCTAACA ATGCGTCTAT CGTCATCTC GGCACCGTCA  
TTGGAATTA CGCCATCAA TAGTGTCAAT TTAAGATTG CGTACGCG TGGACATAC TTTAGATTG TACGCGAGTA GCAGTAGGAG CCGTGGCAGT  
3201 CCCTGGATGC TGTAGGCATA GGCTTGGTTA TGCCGGTACT GCGGGCCTC TTGGG  
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCGGAG AACGC

FIG. 4C

METHODS AND COMPOSITIONS FOR INCREASING  
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3201 CCTTGGATGC TGTAGGATA GGCTTGGTTA TGCCGGTACT GCCGGCCTC TTGCG  
GGGACCTAG ACATCCGTAT CCGAACCAAT ACGGCCATGA CGGCCCGGAG AACGC

FIG. 4D

METHODS AND COMPOSITIONS FOR INCREASING  
ANTIBODY PRODUCTION

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1 ATCGATGAAT TCATGCTGTG GTGTCAATGGT CCGTGATGCG CAGGGTGCCG ACGGSCATCT CGAGTGCACG GTGCACCAAT GCTTCTGGCG TCAGGCAGCC  
TAGCTACTTA AGTACGACAC CACAGTACCA GCCACTAGCG GTCCACGGC TGCGGTAGA GCTGACGTG CACGTGGTTA CGAAGACCGC AGTCCGTCGG  
^ClaI

101 ATCGGAAGCT GTGGTATGGC TGTGCAGGTC GTAATCACT GCATAATTGC TGTGCTCAA. GCGGCACTCC CGTCTGGAT AATGTTTTT GCGCCGACAT  
TAGCCTTGA CACCATACCG ACAGTCCAG CATTTAGTGA CGTATTAGC ACAGGAGTT CCGCGTAGG GCAAGACCTA TTACAAAAA CCGCGCTGTA

201 CATPAACGGT CTGGCAAATA TTCTGAATG AGCTGTGAC AATTAATCAT CGAACTAGTT TAATGTGTG AATGTGTGAC GGATAACAAT TAAGCTTAGG  
GTATTGCCAA GACCGTTTAT AAGACTTTAC TCGACAACTG TTAATTAGTA GCTTGATCA ATTACACACC TTAACACTCG CCTATTGTTA ATTGGAATCC

301 ATTCTAGAGG GAAAGATTAT GAAATCACTG TTAAAGTAA CGCTGCTGGC GACCACAATG GCGGTGCCC TGCATGCACC AATCACTTTT GCTGCTGAAG  
TAAGATCTCC CTTCTAAATA CTTTAGTGAC AAATTTCAIT GCGACGACCG CTGGTGTAC CCGCAACGGG ACGTACGTGG TTAGTGAAAA CGAGCACTTC

1 M K S L F K V T L L A T T M A V A L H A P I T F A A E A  
^fkpA start

401 CTGCAAAACC TGCTACAGCT GCTACAGCA AAGCAGGTT CAAAATGAC GATCAGAAAT CAGCTTATGC ACTGGTGCC TCGCTGGGTC GTTACATGGA  
GACGTTTTGG ACGATGTGCA CGACTGTGCT TTGCTGCGCA GTTTTACTG CTAGTCTTTA TCGAATACG TGACCCACGG AGCGACCCAG CAATGTACCT

29 A K P A T A A D S K A A F K N D D Q K S A Y A L G A S L G R Y M E

501 AACTCTCTA AAAGACAAG AAAAAGCTGG CATCAAACTG GATAAGATC AGCTGATCG TGGTGTTCAG GATGCAITTG CTGATAAGAG CAAACTCTCC  
TTTGAGAGAT TTCTTGTTTC TTTTGACCC GTAGTTTGAC CTATTTCTAG TCGACTAGCG ACCACAAGTC CTAGGTAAAC GACTATCTC GTTTGAGAGG

62 N S L K E Q E K L G I K L D K D Q L I A G V Q D A F A D K S K L S

601 GACCAAGAGA TCGAACAGAC TCTACAAGCA TTGGAAGCTC GCGTGAAGTC TTCTGCTCAG GCGAAGATGG AAAAAGACGC GGCTGATAAC GAAGCAAAAG  
CTGTTCTCT AGCTTGCTG AGATGTTCTG AAGCTTCGAG CCGACTTCAG AAGACGAGTC CCGTCTTACC TTTTCTGCG CCGACTATTG CTTCTGTTTC

95 D Q E I E Q T L Q A F E A R V K S S A Q A K M E K D A A D N E A K G

701 GTAAAGAGTA CCGCGAGAA TTTGCCAAAG AGAAGGTGT GAAACCTCT TCAACTGCTC TGGTTTATCA GGTAGTAGAA GCGGTAAAG GCGAAGCACC  
CATTTCTCAT GCGGCTCTTT AAAGGTTTC TCTTCCACA CTTTGGAGA AGTTGACAG ACCAATAGT CCATCATCTT CCGCCATTTC CGCTTCGTGG

129 K E Y R E K F A K E K G V K T S S T G L V Y Q V V E A G K G E A P

801 GAAAGACAGC GATACGTGTTG TAGTGAATA CAAAGGTACG CTGATCGACG GTAAAGAGTT CGACAACTCT TACACCCGTG GTGAACCGCT TTCTTTCGGT  
CTTCTGTGCG CTATGACAAC ATCACTTGAT GTTTCATGC GACTAGTGC CATTTCTCAA GCTGTTGAGA ATGCGGCAC CACTTGGCGA AGAAGGCA

162 K D S D T V V V N Y K G T L I D G K E F D N S Y T R G E P L S F R

901 CTGGACGGTG TTATCCCGG TTGACAGAA GGTCTGAAGA ACATCAGAA AGGCGGTAA ATCAAACTGG TTATCCACC AGAATGGCT TACGGCAAG  
GACCTGCCAC AATAGGCCCC AACCTGTCTT CCAGACTTCT TGTAGTCTT TCCGCCATT TAGTTGACC AATAAGGTGG TCTTGACCGA ATGCCGTTTC

195 L D G V I P G W T E G L K N I K K G G K I K L V I P P E L A Y G K A

FIG. 5A

1001 CGGCTGTTCC GGGGATCCCA CCGAATTCTA CCCTGTGTT TGACGTAGAG CTGCTGGATG TGAACACAGC GCCGAAGGCT GATGCAAAGC CGGAAGCTGA  
GCCACACAAGG CCCCTAGGGT GGCTTAAGAT GGGACCACAA ACTGCATCTC GACGACCTAC ACTTTGGTCG CGGCTTCOGA CTACGTTTCG GCCTTCGACT  
229 G V P G I P P N S T L V F D V E L L D V K P A P K A D A K P E A D  
1101 TGGCAAGCC GCAGATTCTG CTAAAAATA AAAGCTAGC  
ACGCTTTCGG CGTCTAAGAC GATTTTAT TTTCGATCG  
262 A K A A D S A K K O ^NheI

FIG. 5B

METHODS AND COMPOSITIONS FOR INCREASING  
ANTIBODY PRODUCTION

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1 GAATTCAACT TCCTCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTCTTATTT AAGCTTGCCC AAAAAAGA AGAGTCGAAT  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA  
^EcoRI

101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCTGCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA ACGGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCTCTGA CGACGATAG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA  
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACCA GCTGTCATAA AGTTGTCAAG GCCGAGACTT ATAGTCGCTT TGTCTTTTAT TTTTATGTA TTTGTAATA GTACGCAAGT  
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAATAA AAAATTACAT AAACATTGAT CATGGGTTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAA AAAGAATATC GCATTCTTC TTGATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGCTA CGCTGATATC  
AGTGCATTTT TCCCATAGAT CTTAATACTT TTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTCGCGAT CGCATATAG  
M K K N I A F L L A S M F V F S I A T N A Y A D I  
^start SII signal TIR 7 anti-TF light chain^

501 CAGATGACCC AGTCCCGAG CTCCTCTGCC GCCTCTGCG GCGATAGGCT CACCATCACC TGCAGAGCCA GTCGGACAT CAAAGAGTAT CTGAACTGGT  
GTCTACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCTCGGT CAGCGCTGTA GTTCTCGATA GACTTGACCA  
26 Q M T Q S P S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTA CTATGCTACT AGTCTCGCTG AAGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC  
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCTCAGGG AAGAGGGAAG AGACCTAGGC CAAGACCCCTG  
60 Q Q K P G K A P K V L I Y Y A T S L A E G V P S R F S G S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGCATTGG ACAGGTACC  
CCTAATGTA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGGTTGAA TAATGACAGA AGTCGTGCT CTCAGAGGTA CCTGTAACC TGTCCTATGG  
93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGGTGGAGA TCAACGAAC TGTGGCTGCA CCACTCTGCT TCATCTTCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGC  
TTCCACCTCT AGTTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACGAAGACAA CACACGGACG  
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GGTGATTAAC GGCCTCCAAT CCGGTAATC CCAGGAGAGT GTCACAGAGC AGGACAGCAA  
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATG CCGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGTT  
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 6A



METHODS AND COMPOSITIONS FOR INCREASING  
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1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GAGCTGAGC AAGCAGACT ACGAAGAACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCCTGAGC  
CCTGTGCTGG ATGTCGAGT CGTGTGGGA CTGCGACTCG TTCTCTGA TGTCTTTGT GTTTCAGATG CGGAGCTTC AGTGGTAGT CCCGACTCG  
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S  
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCTT ACGCCGAGC CATCGTGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG  
AGCGGACAGT GTTCTCGAA GTTGTCCTT CACACATTA ATTAGGAGA TCGCGCTGC GTAGCACGC TCGAGCCATG GGGCCCTAGA TCGGATTGC  
226 S P V T K S F N R G E C O  
lambda t0 terminator<sup>\*</sup>  
1201 CTCGGTTGCC GCGGGCGTT TTTTATTGTT GCGAGCGC ATCTGACTG CACGGTGCAC CAATGCTTCT GCGTCCAGC AGCATCGGA AGCTGTGGTA  
GAGCCAACCG CGGCCGCAA AAAATAACAA CCGCTGCGC TAGAGCTGAC GTGCCAGTG GTTAGAAGA CCGCAGTCCG TCGGTAGCCT TCGACACCAT  
1301 TGGCTGTGCA GGTGTAAT CACTGCATAA TTCTGTGCG TCAAGGCGA CTCCGTTCT GGATAATGTT TTTTGGCGC ACATATAAC GGTTCCTGGCA  
ACCGACACGT CCAGCATTTA GTGAGCTATT AAGCACAGC AGTTCGCGT GAGGGCAAGA CCTATTACAA AAAACCGCGC TGTAGTATTG CCAAGACCGT  
1401 AATATTCTGA AATGAGCTGT TGACAATTAA TCATCGAAT AGTTTAAATGT GTGAATGTT GAGCGGATAA CAAATTAAGCT TAGGATCTAG AATTATGAAG  
TTATAAGACT TTAGTCGACA ACTGTAAAT AGTAGCTTGA TCAATTACA CACCTTAACA CTCGCTATT GTTAATCGA ATCCTAGATC TTAATPACTT  
M K  
1 Start STII signal TIR 3<sup>\*</sup>  
1501 AAGAATATTG CGTTCCTACT TGCCTCTATG TTTGCTCTTT CTATAGCTAC AAAGCGTAC GCTGAGTTC AGCTGGTGA GTCTGGCGGT GGCCTGGTGC  
TTCTTATAAC GCAGGATGA ACGGAGATAC AAACAGAAA GATATCGATG TTTGCGATG CGATCCCAAG TCGACCACT CAGACCCCA CCGGACCAAG  
3 K N I A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q  
1601 AGCCAGGGG CTCACTCGT TGTCTCTGT CAGCTTCTGG CTTCATATT AAGGAGTACT ACATGCACTG GGTCTGTCAG GCCCGGGTA AGGCCTGGA  
TCGGTCCCGG GAGTGAGCA AACAGGACAC GTCAAGACC GAAGTTATAA TTCTCATGA TGTACGTGAC CCAGGAGTC CCGGGCCCAT TCCCGGACCT  
37 P G G S L R L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E  
1701 ATGGTTTGA TTGATTGATC CAGAGCAAG CACACAGATC TATGACCGA AGTTCAGGA CCGTCCACT ATAAGCTG ACAATTCAA AAACAGCA  
TACCAACCT AACTAAGTAG GTCTGTTCC GTTGTGCTAG ATACTGGCT TCAAGTCTT GGCAGGTGA TATTCGGAC TGTAAAGTT TTTGTCTCGT  
70 W V G L I D P E Q G N T I Y D P K F Q D R A T I S A D N S K N T A  
1801 TACCTGCAGA TGAACAGCT CCGTGTGAG GACACTGCG TCTATTATTG TGCTGAGAC ACGCCGCTT ACTTCGACTA CTGGGGTCAA GGAACCTGG  
ATGGAGCTCT ACTGTGCGA CGCAGACTC CTGTGACGC AGATAATAAC ACGAGCTCTG TGCCGGCGAA TGAAGCTGAT GACCCAGTT CTTGGGACC  
103 Y L Q M N S L R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V  
1901 TCACGCTCTC CTGCGCTCC ACCAAGGCC CATCGTCTT CCCCTGGCA CCTCTCTCCA AGACACCTC TGGGGSCACA GCGGCCCTGG GCTGCTGCT  
AGTGGCAGAG GAGCCGAGG TGGTCCCGG GTAGCCAGAA GGGGACCGT GAGGAGAGT TCTGTGAG ACCCCGCTGT CCGCGGACC CGACGACCA  
137 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V  
\*Apal  
2001 CAAGGACTAC TTCCCGGAAC CCGTGACGCT GTGCTGGAAC TCAGGCGCC TGACAGCGG CGTGACACCT TTCCCGGCTG TCCTACAGTC CTCAGGACTC  
GTTCTGTATG AAGGGGCTTG GCCACTGCA CAGCACTTG AGTCCGGG ACTGTGCTCC GCAGCTGTG AAGGGCGGAC AGGATGTGAG GAGTCTGAG  
170 K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L

FIG. 6B

METHODS AND COMPOSITIONS FOR INCREASING  
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2101 TACTCCTCTA GCAGCGTGGT GACTGTGCC TCTAGCAGCT TGGGACCCA GACCTACATC TGCAACGTGA ATCACAAGCC CAGCAACACC AAGGTGGACA  
ATAGGGAGT CGTCGCACCA CTGACACGGG AGATCGTGA ACCCGTGGT CTGGATGTAG ACCTTGCACT TAGTGTGG GTCTTTGG TTCACCTGT  
203 Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K  
2201 AGAAAGTTGA GCCCAAATCT TGTGACAAA CTCACACATG CCCACGTGC CCAGCACCTG AACTCTCTGG GGGACCGTCA GTCTTCTCT TCCCCCAAA  
TCTTTCAACT CGGTTTGA ACACTGTTT GAGTGTGTAC GGTGCGACG GGTCTGTGAC TTGAGGACCC CCCTGGCAGT CAGAAGGAGA AGGGGGTTT  
237 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K  
2301 ACCCAAGGAC ACCCTCATGA TCTCCGGAC CCTGAGTGC ACATGGTGG TGTGAGCTG GAGCACGAA GACCTGAGG TCAAGTTCAA CTGGTACGTG  
TGGTTCCTG TGGAGTACT AGAGGCGCTG GGGACTCCAG TGTACGCACC ACCACCTGCA CTCGGTCTT CTGGGACTCC AGTTCAAGTT GACCATGCAC  
270 P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V  
2401 GACGGCGTGG AGGTGCATAA TGCCAAAGACA AAGCGCGGG AGGAGAGTA CAACAGCAG TACCGTGTGG TCAGCGTCTCT CACCGTCTCT CACAGGACT  
CTGCCGACC TCCAGGTATT ACGTTCTGT TTCCGGCGCC TCCTCGTCA TGTGTCGTGC ATGGCACACC AGTCGCAGGA GTGGCAGGAC GTGGTCTCTGA  
303 D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W  
2501 GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA GCGCCCATCG AGAAACCAT CTCCAAGCC AAAGGGCAGC CCGGAGAACC  
CCGACTTACC GTTCTCATG TTCACGTTCC AGAGTTGTT TCGGGAGGT CCGGGGTAGC TCTTTGTA GAGGTTCTGG TTTCCTCTGG GGGCTCTGG  
337 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P  
2601 ACAGGTGTAC ACCCTGCCCC CATCCGGGA AGAGATGACC AAGAACCAGG TCAGCTGTAC CTGCTGTGTC AAAGGTTCT ATCCAGGCA CATCGCGGTG  
TGTCCACATG TGGACGGG GTAGGGCCCT TCTCTACTGG TTCTTGGTCC AGTCGGACTG GACGACCAAG TTTCGGAAGA TAGGTCTGCT GTAGCGGCAC  
370 Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V  
2701 GAGTGGAGA GCAATGGGA GCGGAGAAC AACTACAAGA CCACGCTCC CGTGTGAC TCCGACGGCT CCTTCTCTCT CTACAGCAAG CTCACCGTGG  
CTCACCTCT CGTTACCCGT CCGCTCTTG TTGATGTTT GGTGCGAGG GCAGCCTG AGGCTGCCGA GGAAGRAGGA GATGCTGTTT GAGTGCACCC  
403 E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D  
2801 ACAAGACAG GTGGCAGCAG GGAACCTCT TCTCATGCTC CGTGTGCTG GAGGCTGTG ACAACCACTA CAGCACAAG AGCCTCTCC TGTCTCGGG  
TGTCTCTGTC CACCTGCTC CCCTTGCGA AGATPACGAG GCACTAGTA CTCGAGACG TGTGTGTAT GTGCTGTTT TCGGAGAGG ACAGAGGCC  
437 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G  
2901 TAAATAGCA TGGACGGCC CTAGAGTCCC TAAGCTCGG TTGCGCGCGG GCGTTTITTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT  
ATTATTCGT ACGTGGCGG GATCTCAGG ATTGCGAGC AAGGGCGGCC CGCAAAAAAT AACAACTGT TACAATGAG CGAATAGTAG CTATTGAAA  
470 K O  
3001

FIG. 6C

METHODS AND COMPOSITIONS FOR INCREASING  
ANTIBODY PRODUCTION

Reilly et al. Attorney Docket P1957R1  
Sheet 19 of 33

1 GAATTCAACT TCTCCATPACT TTGGATAGG AATACAGAC ATGAARATC TCATTGCTGA GTTGTTATTT AAGCTTGCC AAAAGAAGA AGACTCGAAT  
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGTCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CCGAGGTAGA AGCTTTGGAG ATTATGCTCA CTGCAATGCT TCGCAATATG GGCAGAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG  
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGCTTAGCA AGCGTTATAC CGCGTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CCGAGTAAAG CCGATGCCA GCATTCTCTGA CGAGTACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA  
CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCTATA AGTTGTACG CCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT  
TTTTCATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAATATGAT AAACATTGAT CATGCGTTCA

401 TCAGGTAAAA AGGTATCTA GAATTATGAA AAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC  
AGTGCATTTT TCCCATAGAT CTTAATACTT TTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I  
^Start STII signal TIR 7 anti-tissue factor light chain^

501 CAGATGACCC AGTCCCGAG CTCCTGTCC GCCTGTGTG GCGATAGGT CACCATCACC TGCAGAGCCA GTCCGAGCAT CAAGAGCTAT CTGAACGTGT  
GTCTACTGG TCAGGGGCTC GAGGGACAG CCGTATCACC GTGCTAGTGG AGTCTCGGT CAGCGCTGTA GTTCTCGATA GACTTGACCA

26 Q M T Q S P S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAAG TACTGATTA CTATGTACT AGTCTGCTG AAGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGGAC  
TAGTTGTCTT TGGTCCCTTT CGAGGCTTTC ATGACTAAT GATACATGA TCAGAGCAC TTCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y Y A T S L A E G V P S R F S G S G T

701 GGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTTGG ACAGGGTACC  
CCTAATGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCTGCTT CTCAGAGGTA CCTGTAAACC TGTCCCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGTGGAGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGTCTCTGTT GTGTGCTGC  
TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATTAATT CTATCCAGA GAGGCCAAG TACAGTGAAC GGTGATAAC GCCCTCCAAT CGGTAACTC CCAGGAGAGT GTACAGAGC AGGACAGCAA  
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CGGGAGTTA GCCCATAGAG GTCCTCTCA CAGTGTCTCG TCCGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCCTCA GCAGCACCT GAGCTGAGC AAAGCAGACT ACGAAGACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCTGAGC  
CCTGCTGG AGTCGGAGT CGTCGGTGGG CTGCGACTCG TTTCCTCTCA TGTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

FIG. 7A

METHODS AND COMPOSITIONS FOR INCREASING  
ANTIBODY PRODUCTION

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1101 TCGCCGCTCA CAAAGAGCTT CAACAGGGA GAGTGTAAAT TAAATCTCT AGCCGGACG CATCTGGGCG AGCTCGGTAC CCGGGGATCT AGGCTAAAG  
AGCGGCAGT GTTCTCGAA GTTGTCCCT CTCACATTA ATTTAGGAGA TCGGCGCTGC GTAGCACCGC TCGAGCCATG GCGCCCTAGA TCCGATTGC  
226 S P V T K S F N R G E C O  
lambda t0 terminator  
1201 CTCGGTTGCC GCGGGGGTT TTTTATTGT GCGACGGC ATCTCGACTG CACGGTGCAC CAATGCTTCT GGCGTCAGGC AGCATCGGA AGCTGTGGTA  
GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGC TAGAGCTGAC GTGCCAGTG GTTACGAGA CCGAGTCCG TCGGTAGCCT TCGACACCAT  
1301 TGGCTGTGCA GGTGCTAAAT CACTGCATTA TTGCTGTGCG TCAAGGCGA CTCCGCTTCT GGATAATGTT TTTTGGCGG ACATCATAAC GGTTCGTGCA  
ACCGACCGT CCAGCATTTA GTGACGTAAT AAGCACAGCG AGTTCCGGT GAGGCAAGA CCTATTACAA AAAACCGCGG TGTAGTATTG CCAAGACCGT  
1401 AATATTCTGA AATGAGCTGT TGACATTAAT TCAATGAACT AGTTTAACT GTGGAATGT GAGCGGATAA CAATTAAGCT TAGGATCTAG AATTATGAAG  
TTATAAGACT TTAATCGACA ACTGTAAAT AGTAGCTTGA TCAATTAACA CACCTTAACA CTGCTTATT GTTAATCGA ATCTAGATC TTAATACATTC  
1 Start M K  
anti-tissue factor heavy chain with cys to ser in hinge  
Start STII signal TIR 3  
1501 AAGAAATATT CGTTCCTACT TGCCTCTATG TTTGCTCTTT CTATAGCTAC AAACGGCTAC GGTGAGTTC AGCTGGTGA GTCTGGCGGT GGCCTGGTGC  
TTCTTATAAC GCAAGGATGA ACGGAGATAC AAACAGAAA GATATCGATG TTTGCGCATG CGACTCCAAG TCGACACCAT CAGACCCCA CCGGACCAAG  
3 K N I A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q  
anti-tissue factor heavy chain with cys to ser in hinge  
1601 AGCCAGGGG CTCACTCGT TGTCTCTGT CAGCTTCTGG CTTCATATT AAGAGTACT ACATGCACTG GGTCTGTCAG GCGCCGGGTA AGGCTGTGA  
TCGTCCCGG GAGTGAGCA AACAGGACAC GTCAAGACG GAAGTTATAA TTCTCTCATGA TGTACGTGAC CCAGGCAGTC CCGGGCCCAT TCCCGGACCT  
37 P G G S L R L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E  
1701 ATGGGTGGA TTGATTGATC CAGAGCAAGG CAACAGATC TATGACCGA AGTTCAGGA CCGTSCCACT ATAAAGCTG ACAATTCCTAA AAACACAGCA  
TACCAACCT AACTAACTAG GTCTGTCTCC GTTGTGCTAG ATACTGGGT TCAAGTCTCT GGACGGTGA TATTGCGAC TGTAAAGTT TTTGTGCTGT  
70 W V G L I D P E Q G N T I Y D P K F Q D R A T I S A D N S K N T A  
1801 TACCTGCAGA TGAACAGCT CCGTCTGAG GACACTGCG TCTATTATTG TGTCTGAGAC ACGGCGCTT ACTTCGACTA CTGGGGTCAA GGAACCTGG  
ATGAGCTCT ACTGTGCGA CGCAGACTC CTGTGACGC AGATAATAC ACGAGTCTG TCGCGGGGAA TGAAGTGTG TGAAGTGTG TGAAGTGTG TGAAGTGTG  
103 Y L Q M N S L R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V  
1901 TCACCGTCTC CTCGGCTCC ACCAAGGGC CATCGTCTT CCGCTGGA CCGCTCTCCA AGAGCACCTC TGGGGGACA GCGGCGCTG GCTGCTGCT  
AGTGCAGAG GAGCGGAGG TGGTCCCGG GTAGCCAGAA GGGGACCGT GGGAGAGGT TCTGTTGAG ACCCGCTGT CCGCGGACC CAGCGGACCA  
137 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V  
2001 CAAGGACTAC TTCCCGAAC CGGTGACGGT GTCGTGAAC TCAGCGGCC TGACACAGCG GTGCACACC TTCCCGGCTG TCCTACAGTC CTCAGGACTC  
GTTCTGATG AAGGGGCTG GCCACTGCA CAGCACCTTG AGTCCGCGG ACTGTGCGC GCAGTGTGG AAGGCGCGAC AGGATGTGAG GAGTCTGAG  
170 K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L  
2101 TACTCCCTCA GCAGGTGGT GACTGTGCC GACTGTGCC TCTAGAGCT TGGGACCCA GACCTACATC TGCAACGTGA ATCAAGCC CAGCAACACC AAGTGGACA  
ATGAGGAGT CGTGCACCA CTGACACGG AGATCTGGA ACCGTGGT CTGGATGTAG ACGTTGACT TAGTGTGCTG GTGCTGTGG TTCCACCTGT  
203 Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

FIG. 7B

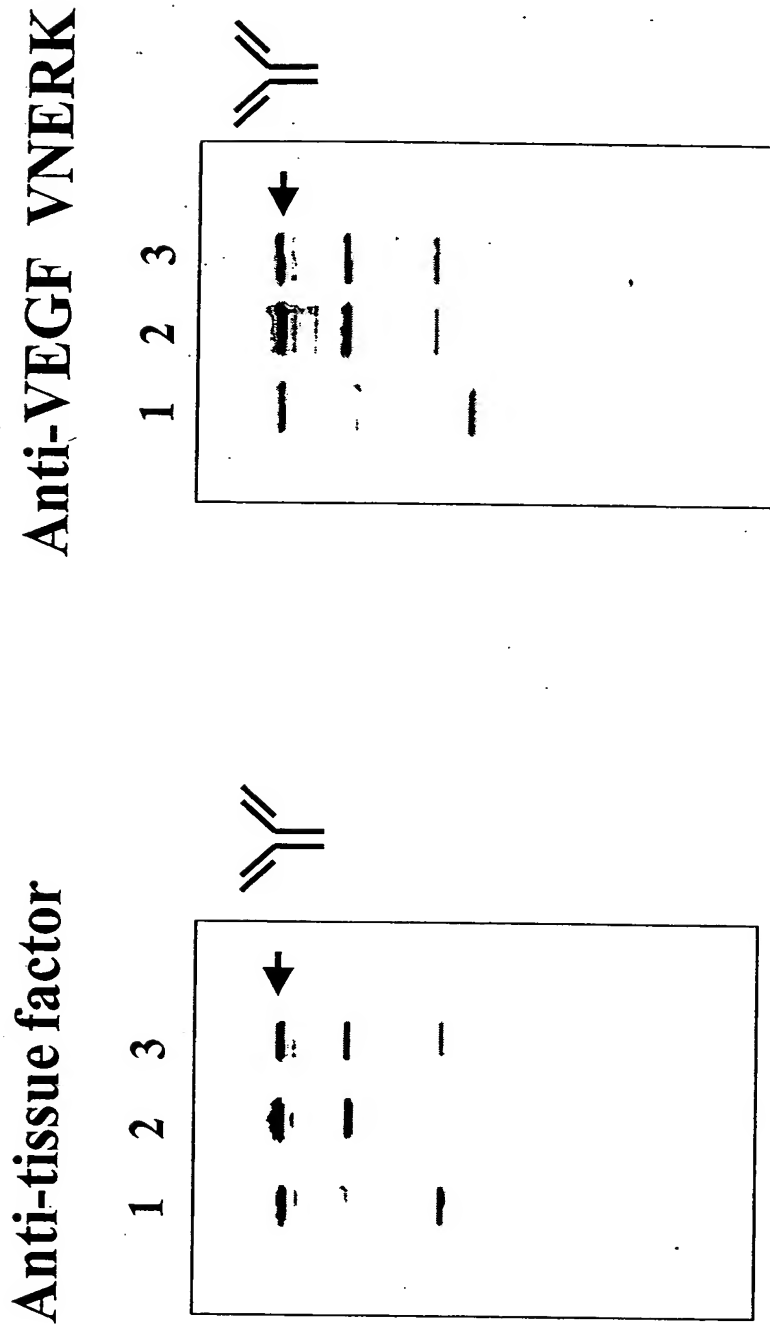
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2201 AGAAGTTGA GCCCAATCT TGTGACAAA CTCACACTAG TCCACCGTCT CCAGCACCTG AACTCTCTGG GGGACCGTCA GTCTTCTCTT TCCCCCAAA  
TCITTCACT CGGGTTTGA ACACGTGTTT GAGTGTGATC AGGTGGCAGA GGTCTGGGAC TTGAGGACCC CCCTGGCAGT CAGAAGAGA AGGGGGTTT  
237 K V E P K S C D K T H T S P P S P A P E L L G G P S V F L F P P K  
^Hinge cys to ser ^Hinge cys to ser  
2301 ACCCAAGGAC ACCCTCATGA TCTCCCGGAC CCTGAGTGC ACATGGGTGG TGGTGGACGT GAGCCACGAA GACCTGAGG TCAAGTTCAA CTGTACGTG  
TGGGTCTCTG TGGGAGTACT AGAGGCCCTG GGGACTCCAG TGTACGACAC ACCACTGCA CTGGTCTCTT CTGGACTCC AGTTCAAGTT GACCATGCAC  
270 P K D T L M I S R T P E V T C V V D V S H E D P E V K F N W Y V  
2401 GACGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG AGGACGACTA CAACAGCAG TACGCTGTGG TCAGCTCTCT CACGCTCTG CACGAGGACT  
CTGCGGCACC TCCACGTATT ACGTTCTGT TTGCGGCGCC TCCTGCTCAT GTTGCTGTGC ATGGCACACC AGTCCAGGA GTGGCAGGAC GTGCTCTTGA  
303 D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W  
2501 GGCTGAATGG CAAGGAGTAC AAGTGAAGG TCTCCAACA AGCCCTCCCA GCGCCCATCG AGAAACCAT CTCNAAGCC AAAGGGCAGC CCGAGAACCC  
CCGACTTACC GTTCTCTCATG TTCAGTTTCC AGAGGTGTTT TCGGGAGGCT CGGGGTAGC TCTTTTGTA GAGGTTTCGG TTTCCTCTCG GGGCTCTTGG  
337 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P  
2601 ACAGGTGTAC ACCCTGCCCC CATCCCGGA AGAGATGACC AAGRACCAGG TCAGCTGAC CTGCTGTGTC AAAGCTTCT ATCCCAGGA CATGCGCGTG  
TGTCCACATG TGGGACGGG GTAGGCCCT TCTCTACTGG TTCTGTGTC AGTCCGACTG GACGGACAG TTTCGAAGA TAGGTCGCT GTAGCGGAC  
370 Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V  
2701 GAGTGGGAGA GCAATGGCA GCGGAGAAC AACTACAAGA CCAGCCTCC CGTGTGGAC TCCGACGGCT CCTTCTTCT CTACAGCAAG CTCACCGTGG  
\*CTCACCTCT CGTTACCCGT CGGCTCTTGG TTGATGTTCT GGTGCGGAGG GCACGACCTG AGGCTGCCGA GGAAGAAGA GATGCTTTC GAGTGGCACC  
403 E W E S N G Q P E N N Y K T T P P V L D S D G S F L Y S K L T V D  
2801 ACAAGAGCAG GTGGCAGCAG GGGAACGTCT TCTCATGCTC CGTGATGCAT GAGGTCTGC ACAACCACTA CACGACAGAAG AGCTCTCTCC TGTCTCCGGG  
TGTCTCTGTC CACCGTCGTC CCTTGCAGA AGAGTAGGAG GACTACGTA CTCGAGACG TGTGTGTGAT GTGCTCTTTC TCGGAGAGG ACAGAGGCC  
437 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G  
2901 TAAATAAGCA TGGGACGGCC CTAGAGTCCC TAAAGTCCG TTGCGCGCGG GGGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT  
ATTATTCTGT ACGCTGCCGG GATCTCAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAAT AACAAATTAG TACAACTGT CGAATAGTAG CTATTGAAA  
470 K O  
3001

FIG. 7C



**FIG. 8**

Anti-tissue factor      Anti-VEGF-VNERK

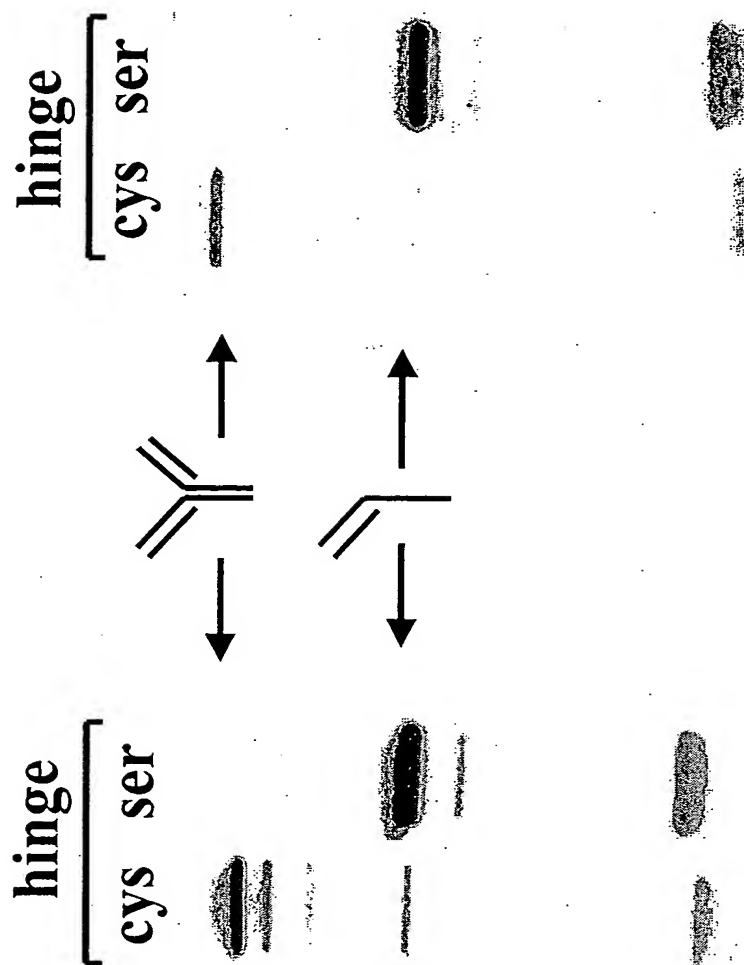


FIG. 9

Anti-VEGF-Y0317

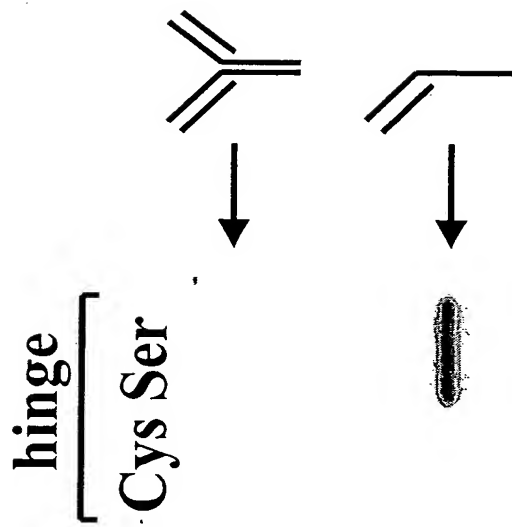


FIG. 10



murine F1t-IgG2b

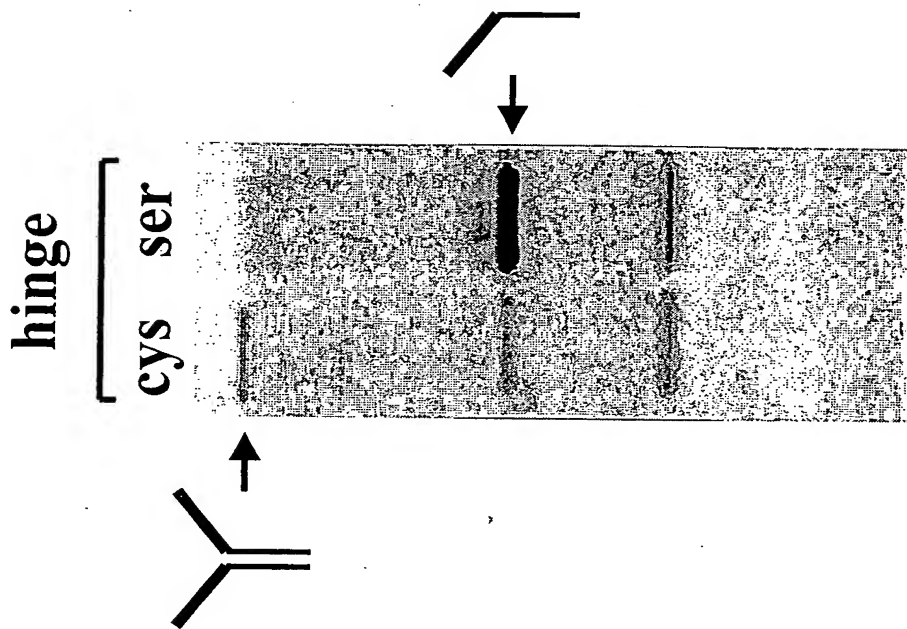


FIG. 11

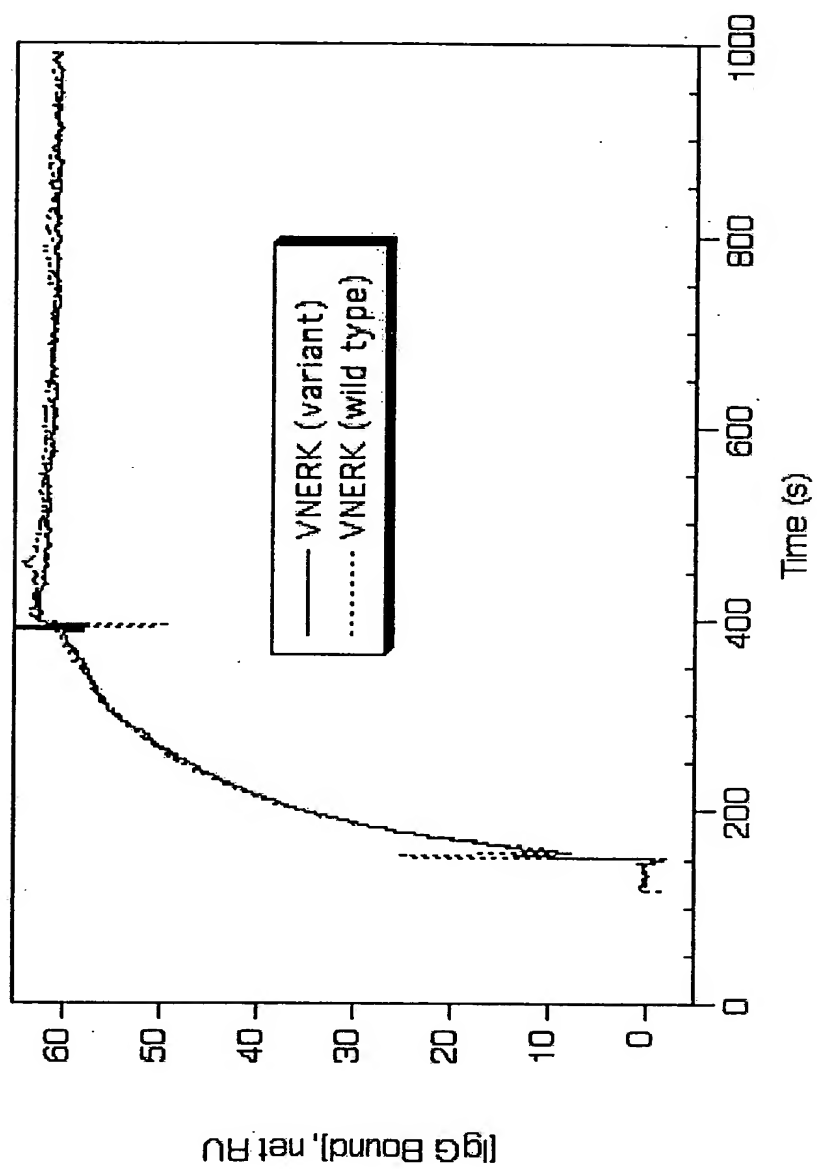
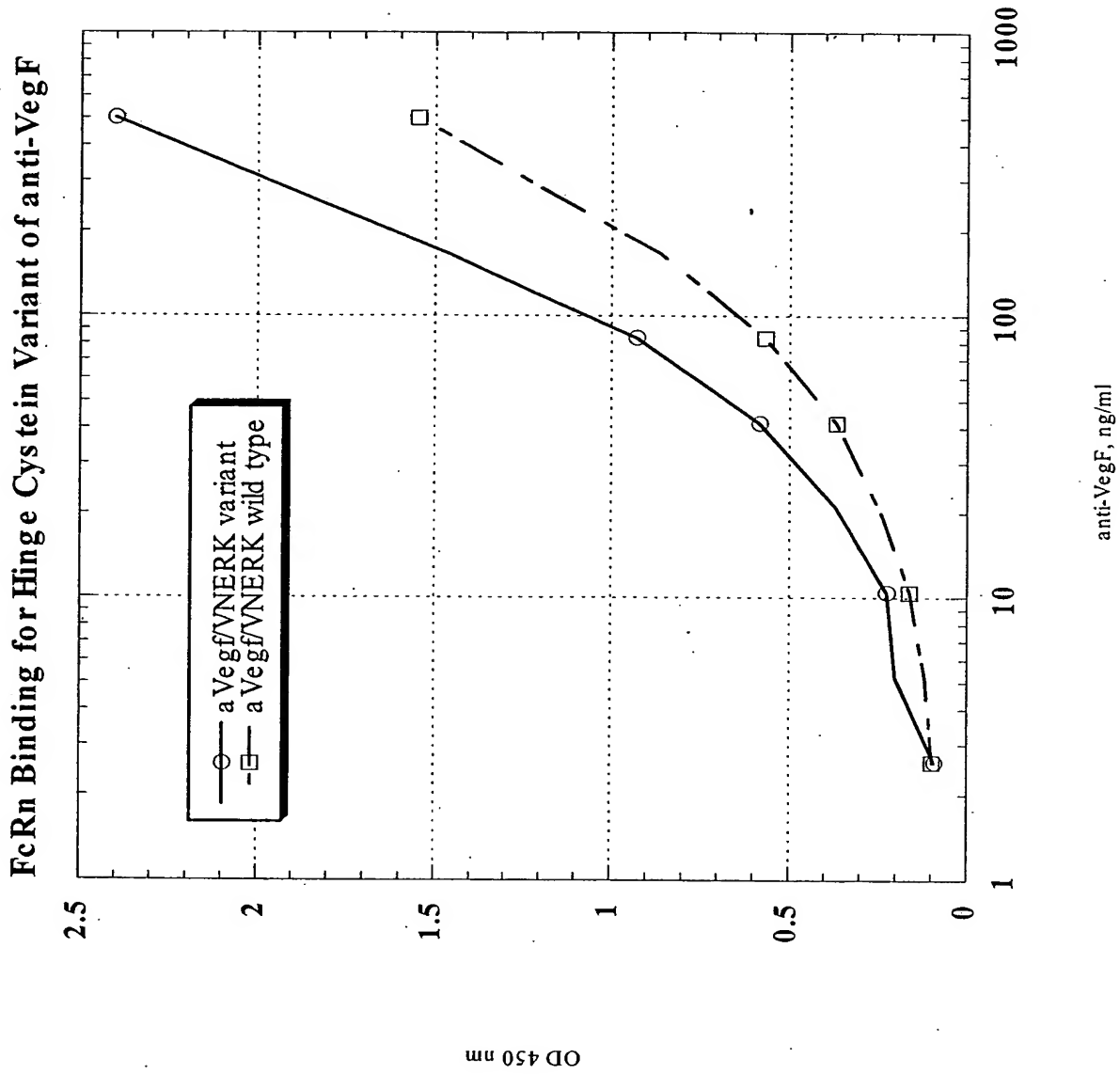
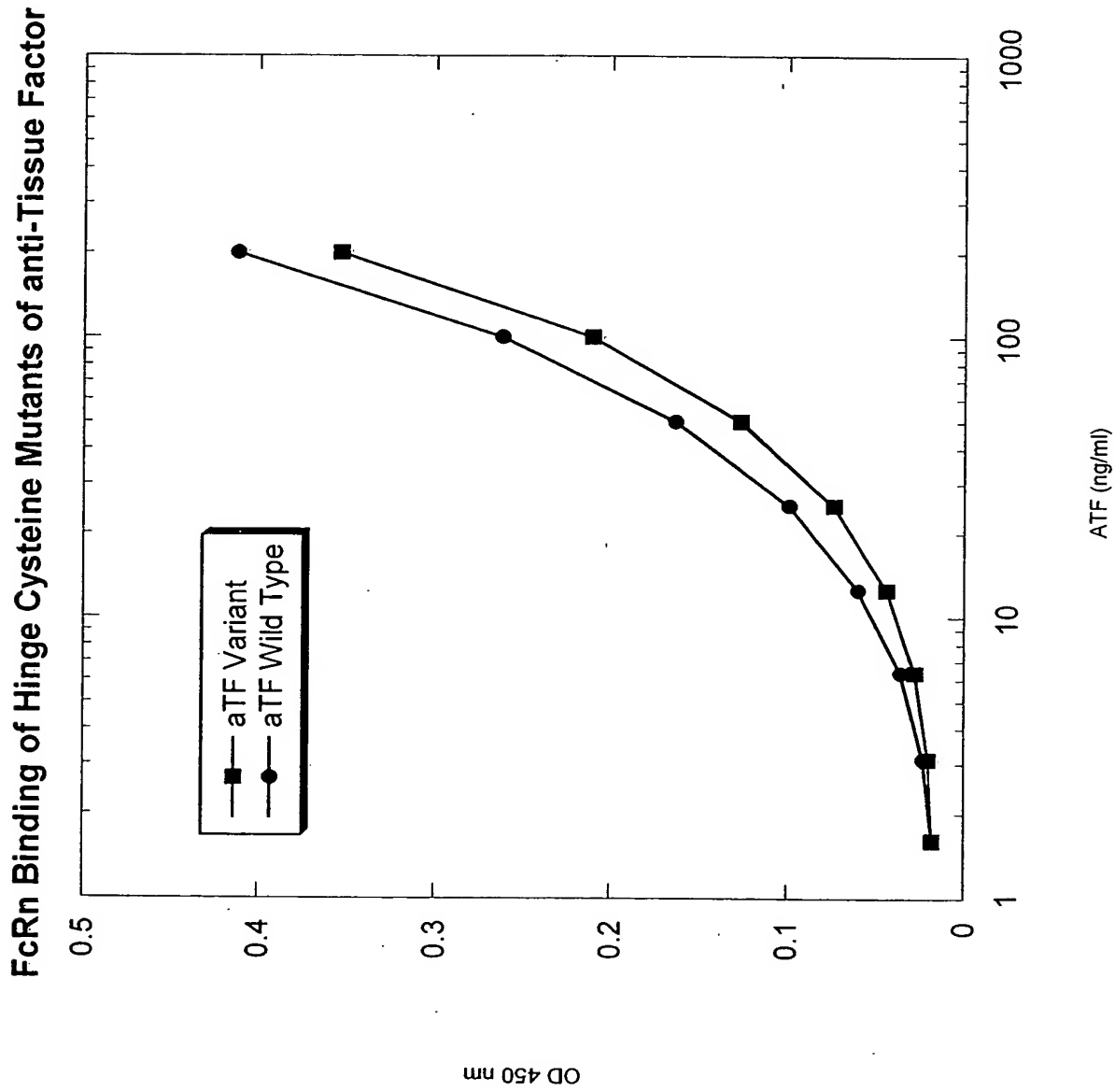


FIG. 12



**FIG. 13**



**FIG. 14**

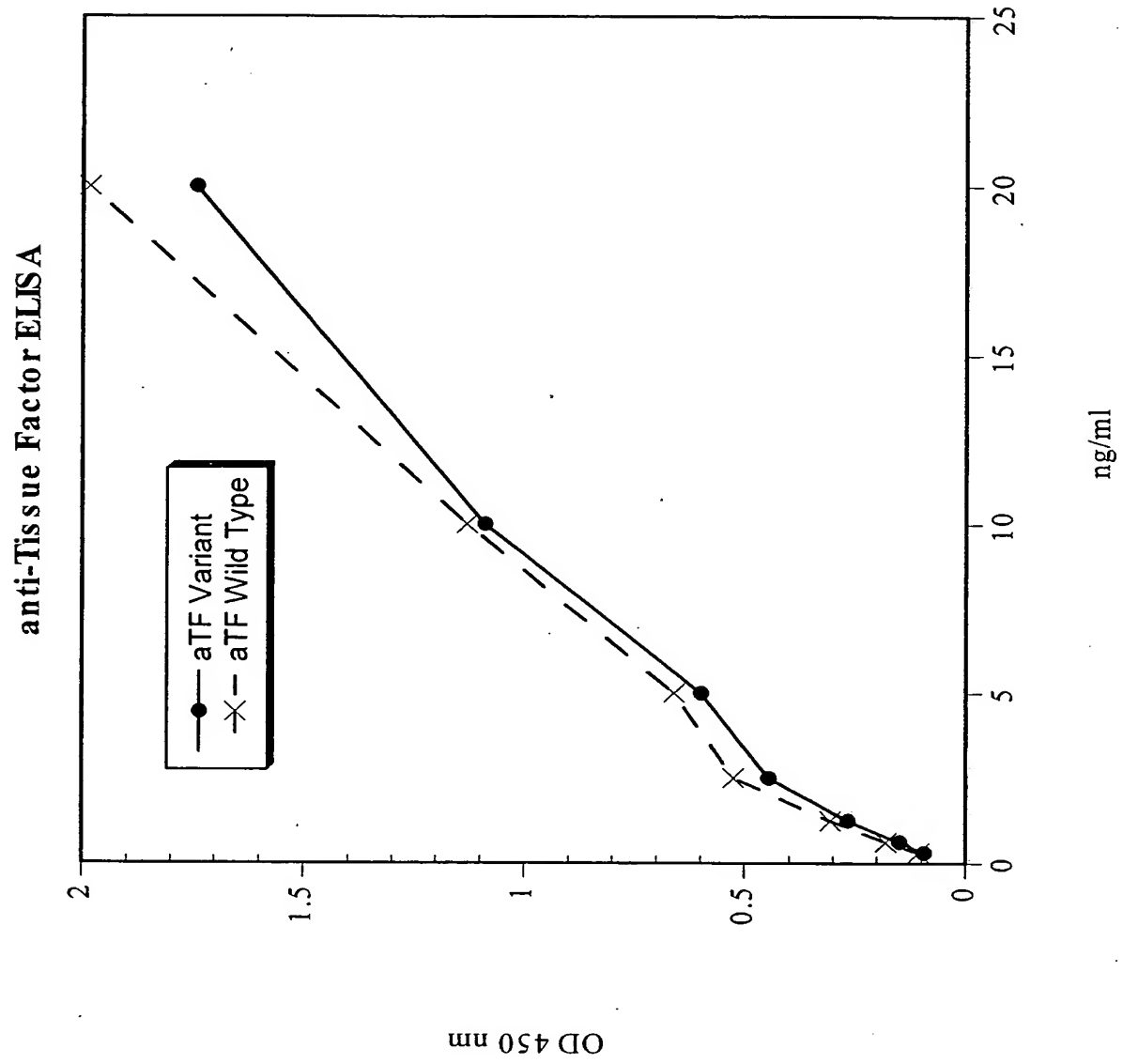


FIG. 15

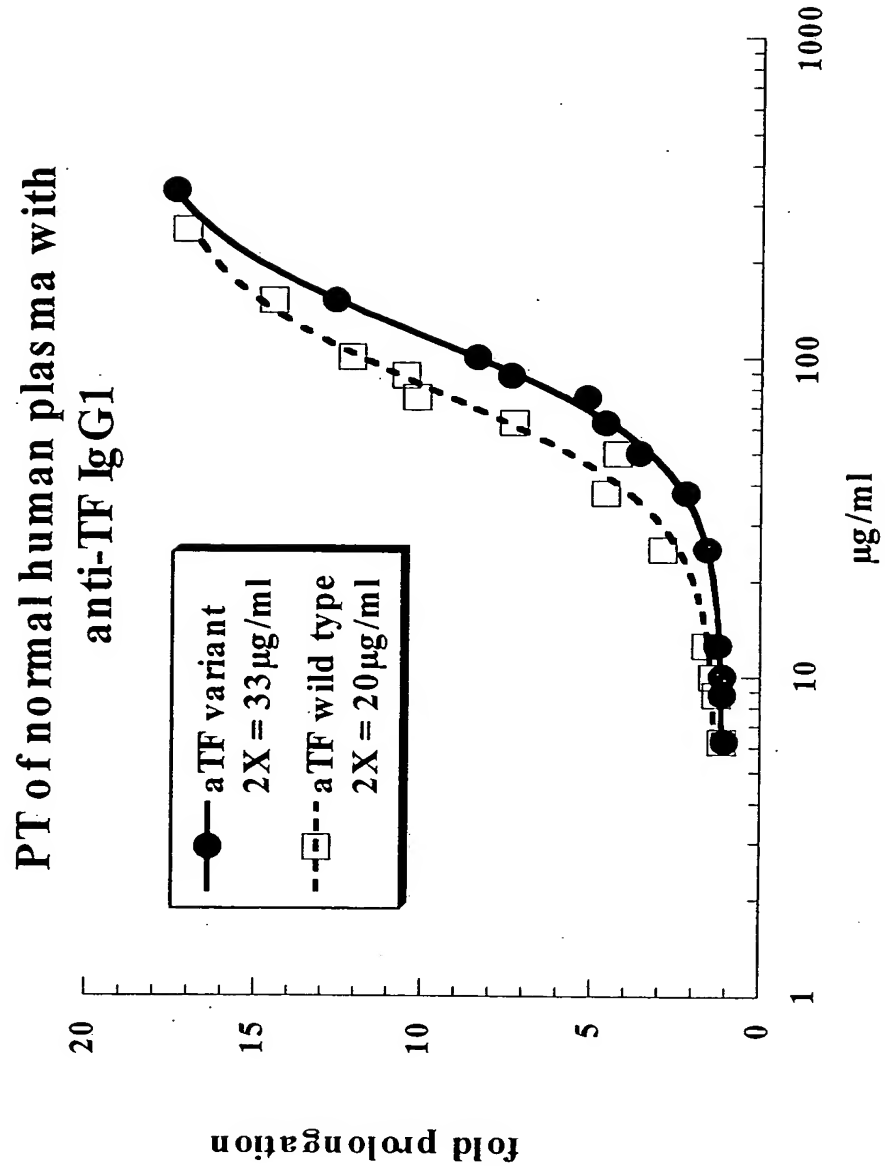


FIG. 16

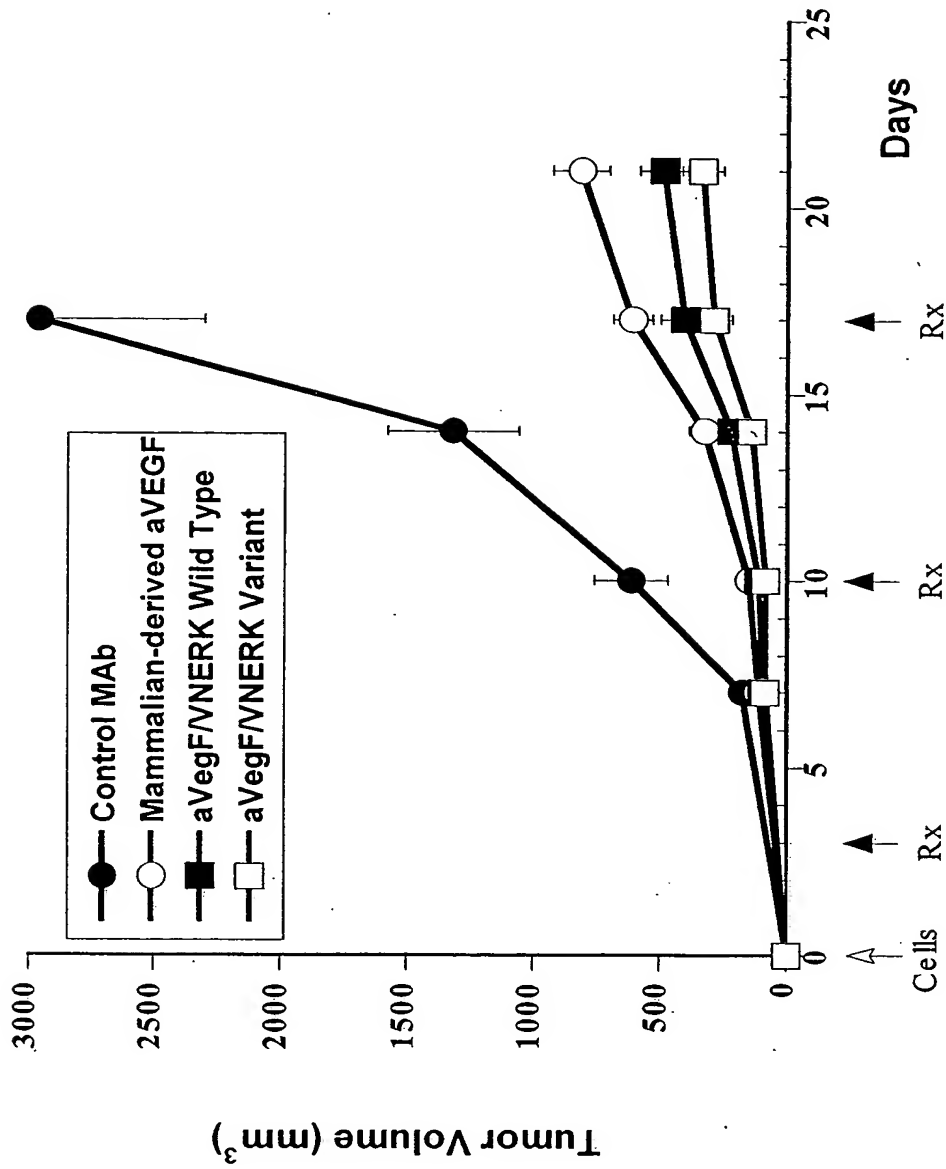


FIG. 17

## Inhibition of Growth of A673 Tumors

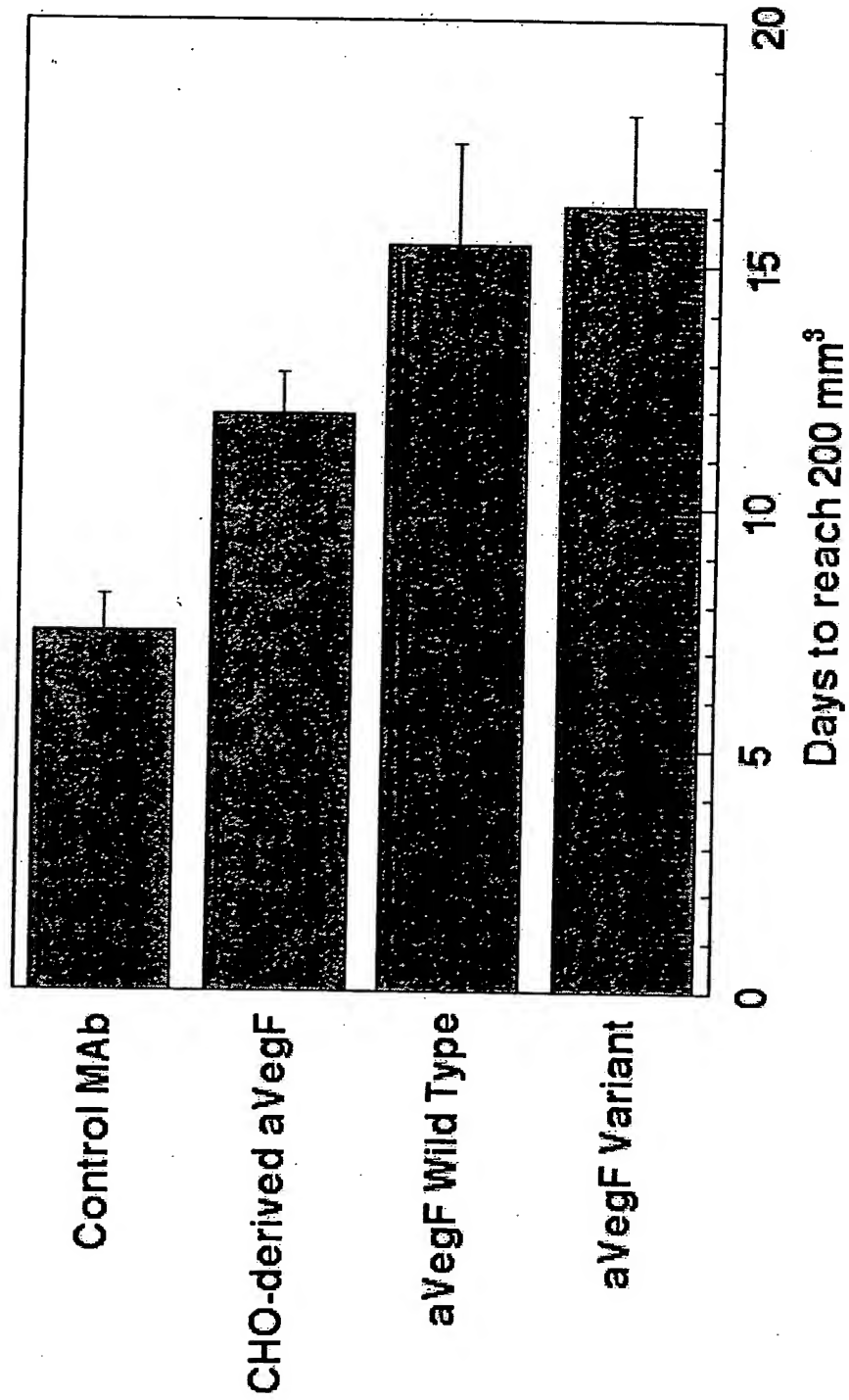


FIG. 18



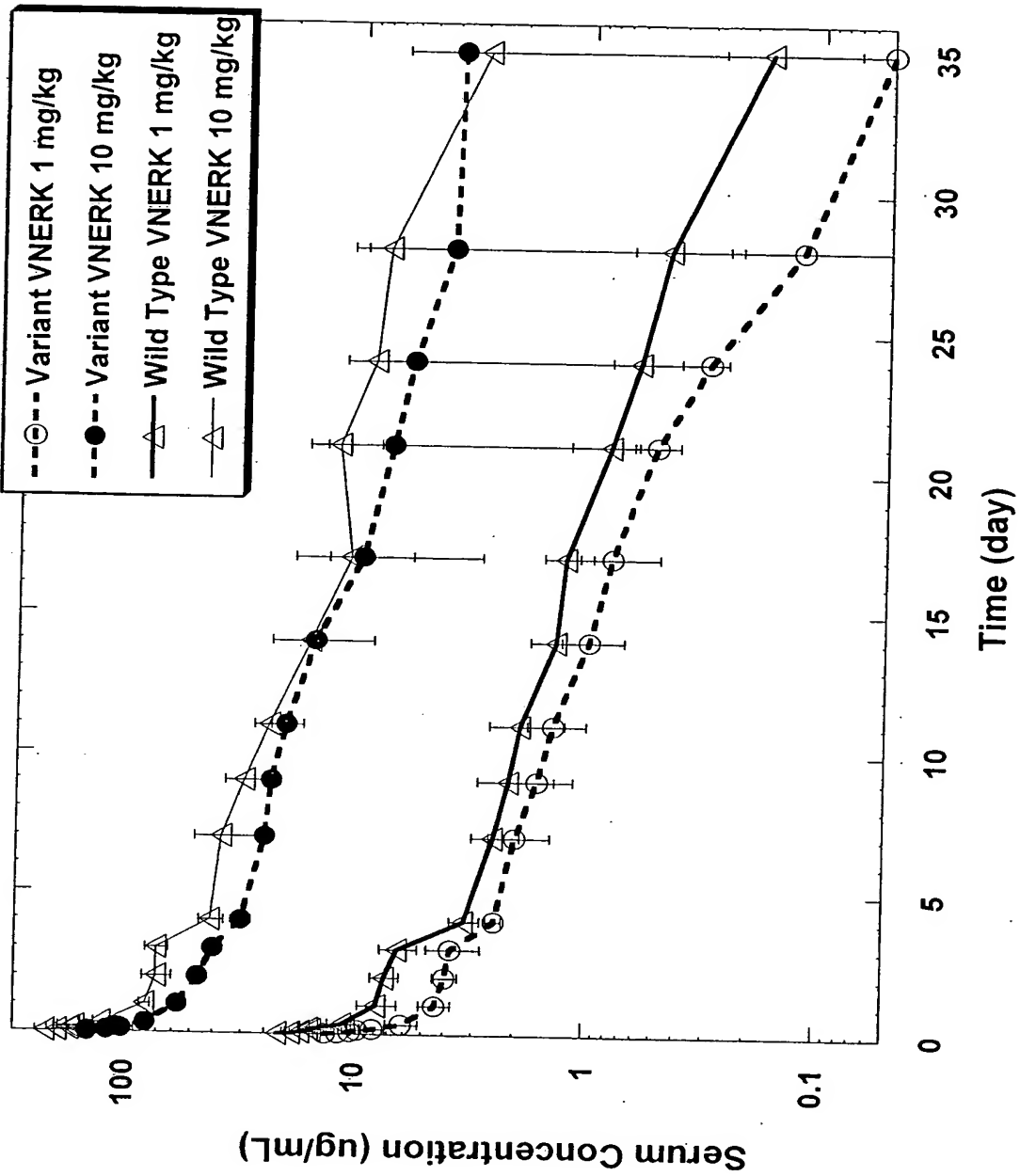


FIG. 19